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APPENDIX D

Evaluation of the Influence of 12 Heparinoid
Derivatives on Thrombin Generation



EVALUATION OF THE INFLUENCE OF 12 HEPARINOID DERIVATIVES ON THROMBIN GENERATION

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A large, handwritten signature in black ink, appearing to read "Prof. MM. Samama". It is heavily stylized and includes a large 'X' drawn through it.

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3134 '04 FEB 20 P3.01

February 20, 2004

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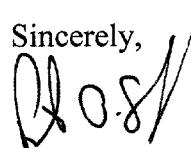
Re: 03P-0064/SUPP 1

Ladies and Gentlemen:

On February 12, 2004, on behalf of Aventis Pharmaceuticals Inc. ("Aventis"), we filed a supplement (the "Supplement") to Aventis' Citizen Petition of February 19, 2003 (03P-0064/CP1). We understand that FDA filed the Supplement to that docket as 03P-0064/Supp 1.

The Supplement contains several reports of preclinical studies, included as Appendices A through I. Several pages of those reports bear "confidential" or "strictly confidential" stamps. Please be advised that these stamps should have been removed prior to submission of the Supplement, and are included on those documents in error. Aventis does not consider this material to be confidential at this time. Therefore, on behalf of Aventis, we request that you treat all of the materials accompanying the Supplement as non-confidential material.

Thank you for your attention to this matter. Please do not hesitate to contact me should you have any questions. Thank you.

Sincerely,

Peter O. Safir



EVALUATION OF THE INFLUENCE OF 12 HEPARINOID DERIVATIVES ON THROMBIN GENERATION

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Introduction:

The biological evaluation of the potential anticoagulant effect of new drugs is based on coagulation tests profiles. This includes global assays such as prothrombin time (PT) or International Normalized Ratio (INR), activated Partial Thromboplastin Time (aPTT) and specialized assays dedicated to investigate well defined targets such as anti-Xa or anti-IIa activities.

However, this approach may lack of accuracy as coagulation is a complex process including positive and negative feedback loops as displayed in figure 1. Thrombin plays a central role in the coagulation cascade, and although some drugs have specific targets different from thrombin, such as specific factor Xa inhibitors, they may induce an inhibition of the thrombin generation. This is for example the case for the indirect, *i.e.* antithrombin dependent, synthetic pentasaccharide fondaparinux (Arixtra®) and for the direct, *i.e.* antithrombin independent, DX-9065a factor Xa inhibitors [1, 2]. This property may be involved in the anticoagulant properties of anticoagulant drugs and the assay may be useful in the *in vitro* assessment of these compounds.

Different assays are available in order to assess the effect of anticoagulant drugs on thrombin generation, including a fluorogenic method allowing this determination in platelet rich plasma.

Results obtained *in vitro* at an early stage of pentasaccharide development demonstrated that this specific and pure anti-Xa compound is unable to suppress completely thrombin generation, but induces a maximal inhibition limited to 80% [3, 4, 5, 6]. Thrombinography or study of thrombin generation is the present reference assay for the evaluation of thrombin generation ; this method takes into account the kinetics and the amount of non neutralized thrombin formed all the time using a dedicated software.

Aventis has developed 12 heparinoid compounds, belonging to two different families, namely DIA2844 and WSD3093. These compounds differ from the length of the oligosaccharides sequence *i.e.* hexasaccharide, octasaccharide, decasaccharide, dodecasaccharide, < hexadecasaccharide and ≥ hexadecasaccharide.

It is admitted that all anticoagulant drugs may inhibit thrombin generation. The antithrombotic activity associated to an antithrombin dependent anti-Xa activity appears only for a number of saccharidic units with a molecular weight ≥ 5,400 D, *i.e.* 16 to 18 saccharidic units. Therefore, it is interesting to compare the thrombin inhibition induced by derivatives containing less than 16 saccharidic units to that induced by derivatives containing 16 or more derivatives. Results obtained for these two families of fractions, which mainly differ by the presence (for compounds containing 16 or more saccharidic units) or absence (for compounds containing less than 16 saccharidic units) of an antithrombin activity, although they exhibit quite a similar anti-Xa activity may be instructive.

On the other hand, hexa-, octa-, deca-, and dodecasaccharide fractions were studied separately and the interpretation of the results should take into account the anti-Xa and anti-IIa properties of these fractions.

The aim of this study is to compare the anticoagulant effect of these compounds evaluated as the inhibition of thrombin generation, as compared to enoxaparin, considered as the reference preparation.

Material and methods:

Reference material:

WSD3093 compounds:

- Hexasaccharide
- Octasaccharide
- Decasaccharide
- Dodecasaccharide
- < Hexadecasaccharide
- \geq Hexadecasaccharide

and

DIA2844 compounds:

- Hexasaccharide
- Octasaccharide
- Decasaccharide
- Dodecasaccharide
- < Hexadecasaccharide
- \geq Hexadecasaccharide

were provided by Aventis as powders.

► Enoxaparin (batch # 314901) was also provided by Aventis as powder.

Thrombin generation assay:

Thrombin generation was assessed using the Thrombogram-Thrombinoscope assay developed by Hemker *et al.* [7, 8].

Principle of the assay:

The method consists of a study of the generation of thrombin, in real time, after recalcification of platelet rich plasma (PRP) in presence of tissue factor (TF) provided by a thromboplastin solution.

The thrombin amidolytic activity on a fluorogenic substrate is then measured.

The quantification of thrombin generated during a 45-minute period of observation is performed *via* the evaluation of the amidolytic activity by measurement of fluorescence, by comparison to a thrombin activity of a thrombin calibrator supplied by SYNPASE.

The determination of thrombogram on PRP moves closer to conditions of the physiological haemostasis than the one performed on platelet poor plasma.

The rationale for the use of different dilutions of thromboplastin is based on the fact that:

- (i) in *in vivo* conditions only trace amounts of tissue factor are present to trigger coagulation,
- (ii) large amounts of thromboplastin may occult any anticoagulant activity leading to a poor sensitivity of the assay, and

- (iii) in contrast low concentrations or total absence of thromboplastin may lead to a highly sensitive system in which low concentrations of the anticoagulant drug may induce an *in vitro* "over-anticoagulation" and lead to ininterpretable results, the power of the anticoagulant drug playing a major role in this response.

Parameters of the thrombogram:

The software calculates the following parameters from thrombogram:

1. Lag-time :

It is the time required for a deviation superior to two standard-deviations of the fluorescent signal from the base line.

This parameter, informative for the phase of initiation of thrombin generation, is expressed in minutes.

2. Endogenous thrombin potential (ETP) :

It is the area under the curve. It represents the complete kinetics of thrombin generation in time.

This parameter allows to appreciate the quantity of thrombin generated and the time of its presence under active form in plasma.

3. Time to peak :

It is the time required for the generation of the maximal quantity of thrombin.

It is expressed in minutes.

4. Time to peak – lag time :

This parameter estimates the time to reach the peak once the reaction has started.

5. Start tail :

It is the time required, expressed in minutes, so that the thrombin concentration returns to zero.

Reagents for the thrombin generation assay:

- i. Fluorogenic Substrate supplied by BACHEM , ref I-1140.0250.
- ii. DMSO supplied by SIGMA, ref D-8418.
- iii. HEPES supplied by SIGMA, ref H-7523.

- iv. Calcium chloride Anhydrous supplied by SIGMA, ref C-4901.
- v. Sodium chloride, 99,5% pure, supplied by MERCK, ref K-30005704.
- vi. Hemoliance-Recombiplastin supplied by Instrumentation Laboratory, ref 49732750.
- vii. 96 well plate (transparent polypropylene round bottom plate) supplied by Greiner, ref 650204.
- viii. Thrombin Calibrator supplied by Synapse BV.
- ix. Citrated Vacutainer supplied by BECTON DICKINSON, 129 mmol/L Citrated Natrium under 0,5 mL, ref 367704.

Reagents preparation:

1. Working buffer:

Hepes buffer (pH7.35,20mM Hepes), 140mM NaCl, BSA 5mg/mL.
For 1L, weigh 4.790 g d'Hepes, 8.223g NaCl and 5.208g BSA. Mix the different weighed in an 1 liter gauged phial and adjust with some distilled water.

This solution will be used for the preparation and the dilution of reagents.

Stability: 1 month, +4°C.

2. Fluo-buffer:

Hepes buffer (pH 7.35, 20mM Hepes), BSA 60mg/mL, sodium azide 0.02%.

For the preparation of Fluo-buffer it is necessary to add 6 g of BSA in 100 mL. Shake slightly during one hour. Then filter the preparation. The preparation is then aliquoted and frozen at -20°C.

Stability : 1 month, -20°C.

3. CaCl₂, 1 M:

In a 200mL gauged phial, introduce 23.125 g of beforehand weighed CaCl₂ and adjust with distilled water.

4. Washing buffer :

Mix 1 CaCl₂ 1M volume solution with 9 distilled water volumes.

5. Fluorogenic substrate:

Z-Gly-Gly-Arg-AMC I-1140 (Bachem).

In 3.76 mL of DMSO add 250mg of fluorogenic substrate.

Stability : 1 month, -20°C.

6. FluCa solution:

In 1750 μL of Fluo-Buffer, add 200 μL CaCl₂ 1M. After 2-3 minutes, add 50 μL of fluorogenic substrate solution (100mM).

Stability: 1 month after preparation.

7. Thrombin standard by Synapse

Dissolve the flask contents in 1 mL of distilled water.

Stability 1 month, -20°C.

8. Hemoliance-Recombiplastin

Dissolve the flask content in 5 mL of physiological water.

Stability : 15 days, +4°C.

All the samples will be tested with 3 following ones Hemoliance-Recombiplastin solutions:

- . 1/40th Hemoliance-Recombiplastin diluted.
- . 1/100th Hemoliance-Recombiplastin diluted.
- . 1/200th Hemoliance-Recombiplastin diluted.

The indicated dilutions are the Hemoliance-Recombiplastin initial dilutions and do not take into account the final dilution (20 μL of Hemoliance-Recombiplastin solution + 80 μL of plasma). Therefore, final dilution are 5-fold higher i.e. 1/200th, 1/500th, and 1/1000th.

9. Heparinoïds concentration ranges in PRP:

9. a. Enoxaparin concentration range in PRP:

In a 25 mL gauged phial, introduce 10 mg of beforehand weighed enoxaparin and adjust with distilled water so as to obtain a 400 $\mu\text{g} / \text{mL}$ enoxaparin stock solution in distilled water.
Store the enoxaparin solution at +4°C.

Prepare three enoxaparin working solutions as follows:

- 200 $\mu\text{g} / \text{mL}$ enoxaparin solution: 1000 μL of the 400 $\mu\text{g} / \text{mL}$ enoxaparin solution + 1000 μL of distilled water.
- 100 $\mu\text{g} / \text{mL}$ enoxaparin solution: 500 μL of the 400 $\mu\text{g} / \text{mL}$ enoxaparin solution + 1500 μL of distilled water.
- 50 $\mu\text{g} / \text{mL}$ enoxaparin solution: 250 μL of the 400 $\mu\text{g} / \text{mL}$ enoxaparin solution + 1750 μL of distilled water.

- 20 $\mu\text{g} / \text{mL}$ enoxaparin solution: 100 μL of the 400 $\mu\text{g} / \text{mL}$ enoxaparin solution + 1900 μL of distilled water.
- 10 $\mu\text{g} / \text{mL}$ enoxaparin solution: 50 μL of the 400 $\mu\text{g} / \text{mL}$ enoxaparin solution + 1950 μL of distilled water.
- 5 $\mu\text{g} / \text{mL}$ enoxaparin solution: 25 μL of the 400 $\mu\text{g} / \text{mL}$ enoxaparin solution + 1975 μL of distilled water.

Plasmas used will be added at the rate of 1 volume of working solution for 19 volumes of plasma to be tested (that is 40 μL of working solution + 760 μL of plasma) so as to obtain the Enoxaparine concentrations as following : 10 $\mu\text{g} / \text{mL}$, 5 $\mu\text{g} / \text{mL}$, 2.5 $\mu\text{g} / \text{mL}$, 1 $\mu\text{g} / \text{mL}$, 0.5 $\mu\text{g} / \text{mL}$ and 0.25 $\mu\text{g} / \text{mL}$.

9. b. Others heparinoids concentration ranges in PRP:

For each molecule, prepare the same range of concentrations in PRP.

10. PREPARATION OF PRP:

10.a. Drawing of blood.

Use a sodium citrated plasma, dripped in a Vacutainer tube (nine volumes of blood to one volume of sodium citrate solution). Be sure that the sodium citrate is at least at 15°C.

1 to 2 mL of blood is needed for each curve that you want to measure.

10.b. Centrifugation and platelet count.

Preparation of PPP.

Centrifuge at 2000 g at 15°C immediately after the blood collection. It is advisable to centrifuge twice to remove all platelets.

Preparation of PRP.

Tubes are centrifuged for 10 min at room temperature, at 130 g, at 15 °C.

The PRP is pipetted off after centrifugation and collected.

Platelet count is measured on the BAYER ADVIA 120 counter.

Then, tubes are centrifuged again for 10 min at 2000 g at room temperature.

The PPP is pipetted off and used to **adjust the PRP to 150,000 platelets /µL.**

Example: when the platelet count is 460,000, take 150 µL of PRP and add 310 µL of PPP or any multiplication of these numbers.

Assay procedure:

1. PRP pool preparation :

PRP pool will be prepared from blood obtained from healthy volunteers using sodium citrate as an anticoagulant.

Two citrated Vacutainer tubes (ref BD 367704) will be taken from 20 subjects so as to prepare 80 mL of PRP.

For PRP pool, a test of thrombin generation will be performed in the presence of the Hemoliance-Recombiplastin solutions described above.

2. Calibration :

Well calibrator (Yellow colour): 20 µL of Thrombin calibrator
 80 µL of PRP

3. PRP thrombogram values :

Associated samples well (red colour): 20 μL of Hemoliance-Recombiplastin solution various dilutions SRC (1/40, 1/100, 1/200) and 80 μL of PRP

Two determinations will be made for each Hemoliance-Recombiplastin dilution.

The assay will then be run according to the manufacturer's procedure.

Results:

Influence of the thromboplastin dilution:

The more the thromboplastin is diluted, the more sensitive is the assay for the measurement of the inhibitory activity to the different heparinoid preparations (Table I and figure 2).

Uninterpretable results were observed for the highest dilution (1/200th) of thromboplastin for the highest concentrations of heparinoid compounds.

On the other hand, the difference observed between the compounds was enhanced by a 1/100th dilution of the thromboplastin as compared to the 1/40th dilution, although no detectable signal was observed for the highest concentration (i.e. 10 $\mu\text{g/mL}$) of DIA \geq hexadecasaccharide (total inhibition of thrombin generation).

Therefore we selected the 1/100th thromboplastin dilution.

Comparative effect of the heparinoid compounds on thrombin generation (Table I) :

Lag-time:

Only a minimal effect on lag time was observed with the different heparinoid compounds at the concentration range tested, except for the WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide compounds, which induced a prolongation of the lag time (figure 3).

ETP:

Oligosaccharide (hexa-, octa-, deca-, and dodecasaccharide) and fractions < 16 hexadecasaccharide have a limited effect, inferior to the one of enoxaparin.

WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide induced a higher inhibition of ETP than enoxaparin. The effect was more pronounced with DIA \geq hexadecasaccharide than with WSD \geq hexadecasaccharide.

All the other compounds induced a more limited inhibition of ETP than enoxaparin.

Results for ETP are displayed in figure 4. Table II summarizes results for 1/100th diluted Recombiplastin.

Peak:

WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide induced a more important reduction of the peak than enoxaparin. The effect was more pronounced with DIA \geq hexadecasaccharide than with WSD \geq hexadecasaccharide.

All the other compounds induced a more limited inhibition of ETP than enoxaparin (figure 5).

Time to peak:

WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide induced a more pronounced delay of the time to peak than the other compounds. The response of the WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide were however quite similar (figure 6).

Time to peak – lag time:

WSD \geq hexadecasaccharide induced a prolongation of the time to peak – lag time parameter as compared to the other compounds (figure 7).

Start-tail:

Results were very variable from one compound to another. However, WSD \geq hexadecasaccharide seemed to prolong more the start-tail than the other compounds (figure 8).

Preliminary conclusions (Tables I and II):

The oligosaccharides (hexa-, octa-, deca- and dodecasaccharide) and the < hexadecasaccharide fractions induce a limited inhibition only found for the highest concentrations of thrombin generation as compared to enoxaparin. Furthermore, no difference was observed between the preparation families WSD and DIA.

However, interestingly, two compounds, namely WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide exhibited a more important response than enoxaparin.

The two most relevant parameters are ETP and peak. For these parameters, the effect of DIA \geq hexadecasaccharide could be more important than this of WSD \geq hexadecasaccharide and requires further investigation.

Therefore complementary experiments were decided in order to:

- (i) confirm the finding obtained in the preliminary run for WSD \geq hexadecasaccharide, DIA \geq hexadecasaccharide, and enoxaparin;
- (ii) implement additional concentrations of the compounds in the range of interest according to the preliminary results, using the 1/100th thromboplastin dilution;
- (iii) assess the intra- and inter-individual variation of the response.

Complementary experiments:

Runs were performed using the following WSD \geq hexadecasaccharide, DIA \geq hexadecasaccharide and enoxaparin concentration range: 10 $\mu\text{g} / \text{mL}$, 9 $\mu\text{g} / \text{mL}$,

8 µg / mL, 6.25 µg / mL, 5 µg / mL, 4 µg / mL, 2.5 µg / mL, 1.6 µg / mL, 1 µg / mL and 0.5 µg / mL, and 0 µg / mL.

A run was performed in quadruplicate using the same donor as in the preliminary experiment (table III).

Another run was performed in triplicate using another donor (table II V).

Lag time:

No difference was observed between WSD ≥ hexadecasaccharide, DIA ≥ hexadecasaccharide and enoxaparin for the lag-time in the two subjects (figures 9 and 10). The lag-phase was prolonged in a dose-dependent manner for concentrations equal or higher than 2.5 µg/mL. The lag-phase was prolonged by 31% and 33% for a 5 µg/mL WSD ≥ hexadecasaccharide and DIA ≥ hexadecasaccharide respectively in one subject and 38% and 43% for the other.

ETP:

The results confirmed that WSD ≥ hexadecasaccharide and DIA ≥ hexadecasaccharide had a more pronounced effect than enoxaparin. DIA ≥ hexadecasaccharide seemed to have a higher effect (estimated around 10%) than WSD ≥ hexadecasaccharide, at least for concentrations lower than 8 - 10 µg/mL, the difference between the two preparations being less important for that high concentration, probably due to the limitation of the methodology (figures 11 and 12). ETP was decreased in a dose-dependent manner for concentrations equal or higher than 2.5 µg/mL. ETP was decreased by 58% and 68% for a 5 µg/mL WSD ≥ hexadecasaccharide and DIA ≥ hexadecasaccharide respectively in one subject and 56% and 66% for the other. A 93% and 92% ETP inhibition was obtained for a 10 µg/mL WSD ≥ hexadecasaccharide and DIA ≥ hexadecasaccharide respectively in one subject and 83% and 91% in the other.

Peak:

Only a minimal effect was observed for low concentrations of WSD ≥ hexadecasaccharide and DIA ≥ hexadecasaccharide (< 2 – 3 µg/mL) and the results are difficult to interpret.

The effect of WSD ≥ hexadecasaccharide and DIA ≥ hexadecasaccharide was more pronounced than for enoxaparin for concentrations higher than 4 µg/mL.

DIA ≥ hexadecasaccharide exhibited a slightly higher effect than WSD ≥ hexadecasaccharide (figures 13 and 14).

The peak was decreased in a dose-dependent manner for concentrations equal or higher than 2.5 µg/mL. The peak was decreased by 73% and 79% for a 5 µg/mL WSD ≥ hexadecasaccharide and DIA ≥ hexadecasaccharide respectively in one subject and 63% and 76% for the other. A 97% and 96% peak inhibition was obtained for a 10 µg/mL

WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide respectively in one subject and 92% and 96% in the other.

Time to peak:

No difference was observed between the three compounds WSD \geq hexadecasaccharide, DIA \geq hexadecasaccharide and enoxaparin (figures 15 and 16).

Time to peak was prolonged in a dose-dependent manner for concentrations equal or higher than 2.5 $\mu\text{g/mL}$. Time to peak was prolonged by 66% and 42% for a 5 $\mu\text{g/mL}$ WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide respectively in one subject and 51% and 76% for the other. A 113% and 176% time to peak prolongation was obtained for a 10 $\mu\text{g/mL}$ WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide respectively in one subject and 133% and 151% in the other.

Time to peak – lag time:

No difference was observed between WSD \geq hexadecasaccharide, DIA \geq hexadecasaccharide and enoxaparin (figures 17 and 18).

Time to peak – lag time was prolonged in a dose-dependent manner for concentrations equal or higher than 2.5 $\mu\text{g/mL}$. Time to peak – lag time was prolonged by 88% and 47% for a 5 $\mu\text{g/mL}$ WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide respectively in one subject and 60% and 100% for the other. A 146% and 230% time to peak – lag time prolongation was obtained for a 10 $\mu\text{g/mL}$ WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide respectively in one subject and 157% and 160% in the other.

Start tail:

No difference was observed between WSD \geq hexadecasaccharide, DIA \geq hexadecasaccharide and enoxaparin (figures 19 and 20). Only a minimal effect was observed for the lowest concentrations (less than 5 $\mu\text{g/mL}$). For higher concentrations, a dose-effect prolongation of the start tail was observed. Start tail was prolonged by 34% and 44% for a 5 $\mu\text{g/mL}$ WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide respectively in one subject and 3% and 13% for the other. A 52% and 60% start tail prolongation was obtained for a 10 $\mu\text{g/mL}$ WSD \geq hexadecasaccharide and DIA \geq hexadecasaccharide respectively in one subject and 66% and 50% in the other.

Overall conclusion:

Thrombinography is considered as a reference method to evaluate anticoagulant drugs. The concept of thrombinography involves a global approach of the mechanisms of anticoagulation, which is not limited to supposed well defined targets such as factor Xa or thrombin. Moreover it is an appropriate test for the evaluation of multi-targeted drugs.

Heparinoid fractions may include both anti-Xa and anti-IIa activities, the relative potency of which is closely related to the number of saccharidic units i.e. to the molecular weight of the preparation. Therefore, thrombinography allows the comparison of the thrombin generation inhibition potency of different preparations which may have a similar anti-Xa activity, but which differ from a chemical point of view.

Aventis has developed two families of compounds (WSD 3093 and DIA2844) which both include different fractions, namely hexa-, octa-, deca-, < hexadecasaccharide, and \geq hexadecasaccharide. The aim of this study was to compare the ability of these different preparations to inhibit thrombin generation.

The assay was run in fresh platelet rich plasma which is close to physiological coagulation conditions.

Different dilutions of thromboplastin were used in the preliminary experiments in order to find the most appropriate dilution of thromboplastin which induces a sensitive and interpretable response of the assay for the different compounds.

Our results confirm that enoxaparin inhibits thrombin generation and a clear dose effect relationship was observed.

Oligosaccharides and fractions < hexadecasaccharide exhibit a limited inhibition of thrombin generation as compared to enoxaparin. No difference was observed between the two families of compounds WSD and DIA for these preparations in the assay used in this study.

Interestingly, there is a difference in the response of thrombin generation (extrinsic pathway) for \geq hexadecasaccharide and < hexadecasaccharide compounds, \geq hexadecasaccharide compounds being more active than < hexadecasaccharide preparations. However, the effect is clearly highlighted for concentrations around 2.5 – 5 $\mu\text{g}/\text{mL}$.

\geq hexadecasaccharide fractions are more potent in the thrombin generation inhibition than enoxaparin. This might be correlated to the fact that the assay is not only partially sensitive to the anti-Xa activity, but also very sensitive to the anti-IIa activity. The importance of this characteristic of the assay in its clinical relevance requires further investigation.

The effect is particularly marked for ETP which, as the area under the curve, includes the amount of thrombin formed and the time to form this thrombin. ETP is currently considered as the most robust parameter of the thrombogram. However, a clear effect is also demonstrated for the lag time, the peak, the time to peak and time to peak – lag time. The effect is less clear for the start tail which should be considered as an exploratory end-point and could be more appropriate for direct thrombin inhibitors.

These results are interesting and underline that in this test, for these compounds, the inhibition of thrombin generation is more potent than the inhibition of factor Xa, which does not mean however that it is of clinical relevance.

Finally, the DIA \geq hexadecasaccharide fraction induces a more potent inhibition of thrombin generation than the WSD \geq hexadecasaccharide fraction. The difference observed between these two fractions might be related to the chemical structure of these fractions. These results support that according to their chemical structure, two compounds of comparable molecular weight may exhibit different activities. This difference may be of interest when trying to identify differences between different low molecular weight heparins. However, since the difference between the responses obtained for the two families of compounds remain of low intensity, further investigation seems desirable.

References:

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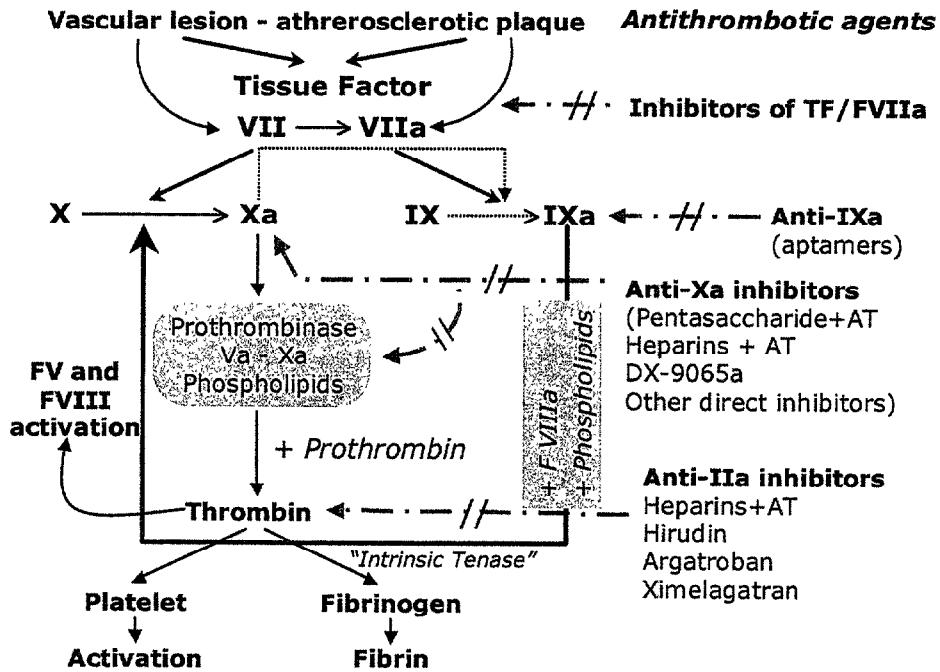


Figure 1 : Coagulation process and antithrombotic drugs

A vascular lesion or the atherosclerotic plaque fracture induces the release of tissue factor, which binds to factor VII activated in factor VIIa. This complex induces the activation of factor X in factor Xa, which, in combination with factor Va, and phospholipids forms the prothrombinase complex. This prothrombinase complex activates prothrombin into thrombin. Thrombin plays a multifactorial and central role in the coagulation process by (i) activating platelets, (ii) transforming fibrinogen into fibrin and by activating factor V and factor VIII in factors Va and VIIIa respectively. In addition, the tissue factor – factor VIIa complex activates factor IX into factor IXa, which, in combination with factor VIIIa and phospholipids forms the “intrinsic tenase” that activates factor X into factor Xa.

The development and the comprehension of the mechanism of action of new antithrombotic drugs is partly based on this concept of the coagulation process.

APPENDICES

WITH HEPARINOID ADDED PRP 1/100 DILUTED																			
	Lagtime	ETP	Peak	UpPeak	Up-LT	startTail	Lagtime	ETP	Peak	UpPeak	Up-LT	startTail	Lagtime	ETP	Peak	UpPeak	Up-LT	startTail	
	1.5	1637	312.5	3.5	2	16	2.25	1583	204.07	6	3.75	21	3.25	1582	159.26	8.5	5.25	24	
	1.5	1661	308.53	3.75	2.25	16	2.25	1621	208.96	6	3.75	21	3.25	1592	160.21	8.5	5.25	23	
	1.5	1638	314.36	3.5	2	16	2.25	1614	210.32	5.75	3.5	20	3.25	1583	175.57	8	4.75	22	
	1.5	1535	315.7	3.5	2	16	2.25	1617	211.37	5.5	3.25	20	3.25	1583	155.84	8.25	5	24	
Mean		150	1617.25	312.77	3.56	2.06	16.00	2.25	1586.25	208.91	5.81	3.56	20.50	3.25	1572.50	162.97	8.31	5.06	23.25
SD		0.00	56.04	3.12	0.13	0.13	0.00	0.00	47.68	3.28	0.24	0.24	0.58	0.00	33.37	8.62	0.24	0.24	0.36
CV %		0	3	1	4	6	0	0	3	2	4	7	3	0	2	5	3	4	
PRP + HEPARINOID 0.25 µg / ml.																			
Tested molecule	With Hemolysis Recombinoplastin 1/100 diluted						With Hemolysis Recombinoplastin 1/100 diluted						With Hemolysis Recombinoplastin 1/200 diluted						
	Lagtime	ETP	Peak	UpPeak	Up-LT	startTail	Lagtime	ETP	Peak	UpPeak	Up-LT	startTail	Lagtime	ETP	Peak	UpPeak	Up-LT	startTail	
Enoxaparin	1.64	1388	278.82	3.46	1.82	16	2.16	1482	211.95	5.01	2.86	20	2.94	1414	176.13	6.67	3.63	21	
Enoxaparin	1.64	1400	278.78	3.46	1.82	16	2.16	1419	214.29	4.75	2.59	18	2.68	1433	180.42	6.31	3.63	21	
Mean	1.64	1383.00	278.30	3.46	1.82	16.00	2.16	1440.50	213.69	4.88	2.72	18.50	2.81	1423.50	172.28	6.44	3.63	21.00	
SD	0.00	24.04	0.74	0.00	0.00	0.00	0.00	30.41	1.73	0.18	0.18	0.71	0.18	13.44	3.03	0.18	0.00	0.00	
CV %	0	2	0	0	0	0	0	2	1	4	7	4	7	1	3	0	0	0	
n versus not heparinoid added PRP %	9	-14	-11	-3	-78	0	-4	-9	2	-16	-67	-5	-14	-9	-23	-56	-10	-10	
WSD3093-Hexasaccharides	1.38	1456	294.34	3.46	2.07	15	2.16	1506	259.38	4.49	2.33	16	2.94	1386	172.26	6.57	3.63	19	
WSD3093-Hexasaccharides	1.64	1487	288.73	3.72	2.08	14	2.16	1541	236.98	4.75	2.59	17	2.68	1391	169.07	6.31	3.63	21	
Mean	1.64	1471.50	282.04	3.59	2.08	14.50	2.16	1523.00	238.18	4.82	2.46	16.50	2.81	1388.50	176.66	6.44	3.63	20.00	
SD	0.18	21.92	3.26	0.18	0.01	0.00	0.00	25.48	1.68	0.18	0.18	0.71	0.18	5.25	2.25	0.18	0.00	0.00	
CV %	12	1	1	5	0	5	0	2	1	4	7	4	7	0	1	3	0	7	
n versus not heparinoid added PRP %	1	-9	-7	1	-75	-9	-4	-4	14	-21	-70	-20	-14	-12	5	-23	-56	-14	
n versus Enoxaparine added PRP %	8	6	5	4	-68	-9	0	6	12	-5	-62	-15	0	0	-4	0	-44	-5	
WSD3093-Octasaccharides	1.64	1580	280.62	3.71	2.07	18	2.16	1605	241.03	5	2.84	20	2.94	1598	205.57	6.81	3.67	19	
WSD3093-Octasaccharides	1.64	1580	285.71	3.71	2.07	17	2.16	1635	238.43	5	2.84	18	2.84	1576	212.26	6.3	3.58	21	
Mean	1.64	1570.00	283.17	3.71	2.07	18.00	2.16	1570.00	248.96	5.86	2.84	18.00	2.84	1587.00	208.92	6.56	3.62	20.00	
SD	0.00	14.14	3.80	0.00	0.00	1.41	0.00	49.50	2.31	0.00	0.00	1.41	0.00	15.56	4.73	0.38	0.18	1.41	
CV %	0	1	1	0	0	8	0	3	1	0	0	7	0	1	2	6	10	7	
n versus not heparinoid added PRP %	9	-3	-6	4	-75	-7	13	-4	15	-14	-66	-7	-10	-4	-25	-57	-14	-14	
n versus Enoxaparine added PRP %	0	14	5	7	-68	-9	13	0	13	-2	-56	-3	5	11	17	2	-44	-5	
WSD3093-Decassaccharides	1.64	1557	304.33	3.45	1.81	16	2.16	1504	245.06	4.76	2.59	18	2.84	1452	189.88	6.3	3.58	20	
WSD3093-Decassaccharides	1.64	1592	287.66	3.71	2.07	23	2.16	1475	228.1	5	2.84	18	2.84	1552	208.83	6.04	3.51	24	
Mean	1.64	1574.50	295.90	3.58	1.94	16.50	2.16	1486.50	258.58	4.88	2.72	18.00	2.84	1502.00	204.26	6.17	3.23	22.00	
SD	0.00	24.75	11.79	0.18	0.16	4.65	0.00	20.51	11.98	0.18	0.18	0.00	0.00	70.71	6.47	0.18	0.18	2.65	
CV %	0	2	4	5	8	25	0	1	5	4	7	0	0	5	3	3	6	13	
n versus not heparinoid added PRP %	9	-3	-5	0	-77	22	-4	-6	13	-16	-67	-7	-10	-4	-25	-57	-14	-14	
n versus Enoxaparine added PRP %	0	14	6	3	-70	22	0	3	11	0	-58	-3	5	15	17	4	-44	-5	
WSD3093-Dodecasaccharides	1.64	1557	248.71	4.24	2.34	18	2.68	1605	183.22	6.06	3.84	23	3.46	1429	118.46	9.95	6.49	27	
WSD3093-Dodecasaccharides	1.64	1553	263.38	4.24	2.34	17	2.68	1495	155.14	6.58	3.9	23	3.46	1490	133.17	9.17	5.71	25	
Mean	1.64	1574.50	265.90	3.58	1.94	16.50	2.16	1550.00	186.18	6.32	3.77	23.00	3.46	1585.00	124.82	9.56	6.10	26.00	
SD	0.00	24.75	10.38	0.00	0.00	0.71	0.18	77.78	19.06	0.37	0.18	0.00	0.00	43.84	11.82	0.55	0.55	1.41	
CV %	0	2	4	5	8	25	0	7	5	12	6	36	0	3	9	6	9	5	
n versus not heparinoid added PRP %	27	-4	-18	19	-72	9	13	-2	-19	8	-55	12	6	-7	-23	15	-27	12	
n versus Enoxaparine added PRP %	16	13	3	23	-64	9	18	3	-21	30	-41	18	23	-30	48	-3	-17	24	
BD3093-Hexadecasaccharides	1.9	1435	257.81	4.24	2.34	19	2.68	1482	184.85	6.06	3.38	28	3.46	1454	122.04	8.4	4.84	28	
BD3093-Hexadecasaccharides	1.9	1523	245.47	4.24	2.34	18	2.68	1428	152.95	6.32	3.64	25	3.46	1337	113.02	8.17	5.71	26	
Mean	1.90	1470.00	241.64	4.24	2.34	18.00	2.68	1480.00	158.80	6.19	3.51	26.50	3.46	1395.50	117.53	8.79	5.33	27.00	
SD	0.00	62.23	5.56	0.00	0.00	0.00	0.00	45.25	8.27	0.18	0.18	2.12	0.00	82.73	6.38	0.64	1.41	1.41	
CV %	0	4	2	0	0	0	0	3	5	3	5	8	0	6	5	6	10	5	
n versus not heparinoid added PRP %	27	-9	-23	19	-72	19	19	-3	-24	6	-58	29	6	-11	-28	6	-36	16	
n versus Enoxaparine added PRP %	16	7	1	23	-64	19	24	1	-25	27	-45	36	23	-34	36	-17	28	28	
>>Hexadecasaccharides	1.25	1464	314.07	3.25	2	15	2.68	1716	245.1	4.76	2.75	30	2.91	1404	153.43	8.08	5.17	17	
>>Hexadecasaccharides	1.5	1774	312.81	3.5	2	24	2	1801	246.84	4.75	2.75	27	2.75	1676	206.05	6.5	3.76	28	
Mean	1.38	1619.00	313.49	3.38	2.00	18.50	2.68	1758.50	245.87	4.75	2.75	28.50	2.81	1526.50	179.74	7.29	4.48	22.50	
SD	0.18	219.20	0.82	0.18	0.00	7.78	0.00	60.10	1.09	0.00	0.00	2.12	0.11	177.48	37.21	1.12	1.00	7.78	
CV %	13	14	0	5	0	42	0	3	0	0	0	7	4	12	21	15	23	35	
n versus not heparinoid added PRP %	-8	0	0	-5	-76	16	-7	11	18	-12	-67	39	-13	-3	10	-12	-31	7	
n versus Enoxaparine added PRP %	-16	17	12	-2	-69	16	-7	22	15	-3	-57	46	23	-57	1	1	13	7	
DM2844-Octasaccharides	1.9	1771	288.43	4.23	2.33	20	2.68	1727	215.7	5.78	3.1	22	3.71	1698	181.14	8.37	4.68	26	
DM2844-Octasaccharides	1.9	1681	301.17	3.87	2.07	16	2.84	1718	208.82	6.04	3.1	23	3.45	1705	178.31	7.59	4.14	26	
Mean	1.90	1731.00	294.88	4.10	2.28	18.00	2.81	1723.00	212.31	5.81	3.10	22.50	3.45	1611.50	138.81	8.73	5.30	26.00	
SD	0.00	56.57	9.01	0.18	0.18	2.83	0.18	5.68	4.79	0.00	0.00	2.12	0.00	67.18	6.20	0.18	0.18	0.71	
CV %	0	3	3	4	8	16	7	0	2	3	0	3	6	0	4	2	3	3	
n versus not heparinoid added PRP %	27	7	6	15	-74	13	25	9	2	2	-63	10	10	8	5	-47	12	24	
n versus Enoxaparine added PRP %	16	25	3	25	-70	16	23	0	-11	8	-58	15	21	5	7	-47	12	24	
DM2844-Decassaccharides	1.9	1634	261.96	4.23	2.33	19	2.68	1676	203.58	5.78	3.1	2							

	Legtime	ETP	Peak	tPeak	IP-LT	startTail	Legtime	ETP	Peak	tPeak	IP-LT	startTail	Legtime	ETP	Peak	tPeak	IP-LT	startTail	
	1,5	1637	312,5	3,5	2	16	2,25	1693	204,07	6	3,75	21	3,25	1682	168,26	8,5	6,25	24	
	1,5	1661	308,53	3,75	2,25	16	2,25	1621	208,86	6	3,75	21	3,25	1692	160,21	8,5	6,25	23	
	1,5	1638	314,36	3,5	2	16	2,25	1614	210,32	6,75	3,5	20	3,25	1593	175,57	9	4,75	22	
	1,5	1535	315,7	3,5	2	16	2,25	1517	211,37	5,5	3,25	20	3,25	1523	158,84	8,25	5	24	
Mean		1,50	1617,25	312,77	3,56	2,08	16,60	2,25	1588,25	208,91	5,81	3,56	20,50	3,25	1572,50	162,97	8,31	5,06	23,25
SD		0,00	56,04	3,12	0,15	0,15	0,00	0,00	47,88	3,28	0,24	0,24	0,58	0,00	33,37	8,52	0,24	0,96	
CV %		0	3	1	4	6	0	0	3	2	4	7	3	0	2	6	3	4	
PRP + HEPARINOID 0,5 µg / mL.																			
Tested molecule	With Hemolance Recombiplastin 1/40 diluted						With Hemolance Recombiplastin 1/100 diluted						With Hemolance Recombiplastin 1/200 diluted						
	Legtime	ETP	Peak	tPeak	IP-LT	startTail	Legtime	ETP	Peak	tPeak	IP-LT	startTail	Legtime	ETP	Peak	tPeak	IP-LT	startTail	
Enoxaparin	1,39	1414	278,68	3,48	2,07	17	1,9	1410	216,08	4,75	2,85	16	2,68	1392	177,08	6,05	3,37	20	
Enoxaparin	1,39	1390	275,92	3,48	2,07	17	1,9	1436	210,2	4,75	2,85	19	2,68	1419	171,7	6,31	3,63	23	
Mean	1,39	1462,00	277,24	3,48	2,07	17,00	1,90	1423,00	213,15	4,75	2,85	17,50	2,68	1405,50	174,39	6,18	3,50	21,50	
SD	0,00	16,57	2,01	0,00	0,00	0,00	0,00	19,30	4,18	0,00	0,00	2,12	0,00	18,09	3,90	0,18	2,12	10	
CV %	0	1	1	0	0	0	0	1	2	0	0	12	0	1	2	3	5	10	
Variation versus not heparinoid added PRP %	-7	-13	-11	-3	-7,5	6	-16	-10	2	-18	-6,6	-15	-18	-11	7	-26	-58	-8	
WSD3093-Hexosesaccharides	1,39	1572	276,2	3,48	2,07	14	2,16	1359	202,31	4,75	2,85	17	2,68	1534	198,38	6,31	3,63	21	
WSD3093-Hexosesaccharides	1,34	1348	272,13	3,48	1,82	16	1,9	1372	212,75	4,75	2,85	15	2,68	1696	203,84	5,25	4	16	
Mean	1,32	1368,00	274,17	3,48	1,85	14,50	2,03	1365,56	207,53	4,75	2,72	16,00	1,97	1585,00	226,01	5,78	3,82	18,50	
SD	0,18	16,57	2,88	0,00	0,18	0,71	0,18	19,30	5,18	0,00	0,18	1,41	1,01	68,27	53,22	0,75	0,28	3,54	
CV %	12	1	1	0	9	6	8	1	4	0	7	9	51	5	24	15	7	18	
Variation versus not heparinoid added PRP %	9	-16	-12	-3	-7,7	-9	-10	-14	-1	-18	-6,7	-22	-40	1	-30	-54	-20	-10	
Variation versus Enoxaparin added PRP %	9	-3	-7	0	-69	-15	7	-4	-3	0	-56	-9	-27	13	30	-6	-38	-14	
WSD3093-Octosesaccharides	1,64	1633	307,48	3,71	2,07	14	2,16	1662	237	5,26	3,1	18	2,04	1683	219,5	6,61	3,67	19	
WSD3093-Octesesaccharides	1,64	1633	310,04	3,45	1,81	16	2,42	1626	238,68	5,26	2,84	18	2,68	1620	214,07	6,3	3,62	20	
Mean	1,64	1633,00	308,78	3,58	1,94	15,00	2,29	1644,00	238,34	5,26	2,97	18,50	2,81	1836,50	216,78	6,56	3,75	19,50	
SD	0,00	0,00	1,81	0,18	0,18	0,41	0,18	26,45	0,23	0,00	0,18	0,71	0,18	23,33	3,84	0,38	0,18	0,71	
CV %	0	0	1	5	8	6	8	2	0	0	6	4	7	1	2	6	4	4	
Variation versus not heparinoid added PRP %	9	-1	-12	-3	-7,7	-9	-10	-14	-1	-18	-6,7	-22	-40	4	-33	-55	-16	-10	
Variation versus Enoxaparin added PRP %	9	-3	-7	0	-69	-15	7	-4	-3	0	-56	-9	-27	13	30	-6	-38	-14	
WSD3093-Decasesaccharides	1,64	1635	266,98	3,71	2,07	21	2,16	1508	237,65	4,75	2,84	21	2,68	1478	204,91	6,3	3,62	20	
WSD3093-Decasesaccharides	1,64	1658	268,01	3,71	2,07	21	2,16	1508	237,82	4,98	2,72	18,00	2,81	1458,00	203,68	6,30	3,48	20,50	
Mean	1,64	1598,50	267,70	3,71	2,07	21,00	2,16	1508,50	237,82	4,98	2,72	18,00	2,81	1458,00	203,68	6,30	3,48	20,50	
SD	0,00	54,45	1,85	0,00	0,00	0,00	0,00	3,54	0,37	0,18	0,18	2,83	0,18	22,28	1,05	0,00	0,18	0,71	
CV %	0	3	1	0	0	0	0	0	0	4	7	15	7	2	1	0	5	3	
Variation versus not heparinoid added PRP %	9	-1	-8	4	-75	31	-4	-5	14	-16	-6,7	-7	-14	-5	26	-58	-12	-12	
Variation versus Enoxaparin added PRP %	9	-3	-7	0	-69	-12	24	14	6	-56	-9	5	7	18	2	-44	-5	-5	
WSD3093-Dodecaesaccharides	1,64	1578	268,82	3,71	2,07	21	2,16	1511	238,08	4,75	2,85	17	2,68	1518	206,4	6,3	3,62	21	
WSD3093-Dodecaesaccharides	1,64	1601	263,98	3,68	2,34	20	2,42	1626	170,64	6,08	3,64	24	3,46	1428	119,07	7,93	4,68	26	
Mean	1,77	1589,50	261,15	4,11	2,34	19,50	2,55	1578,00	183,24	6,18	3,64	22,50	3,33	1502,50	132,94	8,66	5,33	27,00	
SD	0,18	16,26	4,00	0,18	0,00	0,71	0,18	66,47	10,47	0,19	0,00	2,12	0,18	105,36	21,02	1,10	0,91	1,41	
CV %	10	1	2	4	0	4	7	4	8	3	0	9	6	7	16	13	17	5	
Variation versus not heparinoid added PRP %	18	-2	-17	15	-72	22	13	-1	-22	6	-56	10	2	-4	-18	4	-36	16	
Variation versus Enoxaparin added PRP %	18	-3	-13	6	-62	15	34	11	-23	30	-41	29	24	7	-24	40	-14	26	
WSD3093->Hexadesaccharides	1,64	1578	245,72	4,24	2,6	20	2,68	1659	158,63	6,32	3,64	27	3,2	1481	121,72	8,66	5,48	28	
WSD3093->Hexadesaccharides	1,64	1523	247,88	4,24	2,6	17	2,42	1530	167,22	6,06	3,64	27	3,2	1499	123,86	8,17	5,97	28	
Mean	1,64	1550,50	246,80	4,24	2,60	18,50	2,65	1644,50	182,83	6,19	3,64	27,00	3,26	1498,00	122,84	8,82	5,72	28,00	
SD	0,00	38,88	1,63	0,00	0,00	2,12	0,18	20,61	6,07	0,18	0,00	0,00	0,00	127,5	1,58	0,38	0,00	0,00	
CV %	0	3	1	0	0	11	7	1	4	3	0	0	1	1	4	6	0	0	
Variation versus not heparinoid added PRP %	9	-4	-21	19	-69	16	13	-3	-22	6	-56	32	-2	-5	-25	7	-31	20	
Variation versus Enoxaparin added PRP %	9	-11	-23	15	-58	9	34	9	-24	30	-41	54	19	6	-30	44	-8	30	
GD3093->Hexadesaccharides	1,5	1614	316,89	3,5	2	17	2	1576	268,67	4,75	2,75	16	3,43	1579	132,85	8,63	6,2	26	
GD3093->Hexadesaccharides	1,5	1530	324,1	3,25	1,76	14	2	1570	267,81	4,65	2,63	18,00	3,43	1619,00	134,02	9,50	6,07	27,00	
Mean	1,50	1572,00	320,00	3,38	1,88	15,50	2,00	1673,00	267,09	4,63	2,63	0,00	3,43	1619,00	134,02	9,50	6,07	27,00	
SD	0,00	58,40	5,81	0,18	0,18	2,12	0,00	4,24	1,16	0,18	0,00	0,00	0,00	56,57	1,93	0,18	1,41	5	
CV %	0	4	2	5	8	14	0	0	0	4	7	0	0	3	1	2	3	5	
Variation versus not heparinoid added PRP %	9	-3	2	-5	-77	-9	-11	-1	26	-20	-68	-22	6	3	-18	14	-27	16	
Variation versus Enoxaparin added PRP %	9	-2	-7	-2	-70	-9	-11	-1	25	-3	-56	-9	28	15	-23	54	-2	26	
DIA2844-Hexosesaccharides	1,5	1406	284,76	3,5	2	14	1,75	1549	238,82	4,25	2,5	26	2,68	1342	198,6	8,25	5,76	27	
DIA2844-Hexosesaccharides	1,5	1410	291,23	3,25	1,75	18	2	1322	233,76	4,5	2,5	27	2,81	1314	125,59	8,08	5,17	27	
Mean	1,50	1408,00	288,00	3,38	1,88	16,00	1,88	1435,50	238,70	4,38	2,50	21,50	2,71	1328,00	158,10	7,17	4,48	23,00	
SD	0,00	2,83	4,57	0,18	0,18	2,83	0,18	160,51	4,28	0,18	0,00	4,85	0,28	19,80	43,14	1,28	1,00	5,86	
CV %	0	0	2	2	8	18	0	1	2	4	0	23	1	28	18	7	23	25	
Variation versus not heparinoid added PRP %	9	-13	-8	-5	-77	-9	-17	-10	13	-25	-70	5	-17	-10	-4	-14	-1	-23	
Variation versus Enoxaparin added PRP %	9	0	4	-2	-70	-9	-11	-1	11	-6	-60	23	1	-10	-16	-23	-7	-23	
DIA2844-Octosesaccharides	1,5	1688	268,79	4,23	2,33	22	2,94	1580	188,81	6,3	3,36	26	3,45	1634	201,94	7,08	3,63	23	
DIA2844-Octosesaccharides	1,5	1686	278,89																

Lagtime	ETP	Peak	IPeak	IP-LT	startTail	Lagtime	ETP	Peak	IPeak	IP-LT	startTail	Lagtime	ETP	Peak	IPeak	IP-LT	startTail
1,5	1837	312,5	3,5	2	16	2,25	1583	204,07	6	3,75	21	3,25	1582	159,26	6,5	5,25	24
1,5	1821	308,53	3,75	2,05	16	2,25	1621	209,86	6	3,75	21	3,25	1582	160,21	6,5	5,25	23
1,5	1636	314,36	3,5	2	16	2,25	1614	210,32	5,75	3,5	20	3,25	1589	175,57	8	4,75	22
1,5	1535	315,7	3,5	2	16	2,25	1517	211,37	5,5	3,25	20	3,25	1523	156,84	8,25	5	24

Mean
SD
CV %

1,50
0,00
0

1817,25
56,04
3

312,77
3,12
1

3,56
0,13
4

2,06
0,13
6

16,00
0,00
0

2,25
0,00
3

1598,25
47,88
2

208,81
3,28
4

5,21
0,24
7

3,56
0,24
9

20,80
0,58
1

3,25
0,58
3

1572,50
33,37
2

162,97
8,52
5

8,31
0,24
3

5,08
0,24
5

23,25
0,24
4

PRP + HEPARINOID 1 µg / mL.																		
Tested molecule	With Hemolance Recombiplastin 1/40 diluted						With Hemolance Recombiplastin 1/100 diluted						With Hemolance Recombiplastin 1/200 diluted					
	Lagtime	ETP	Peak	IPeak	IP-LT	startTail	Lagtime	ETP	Peak	IPeak	IP-LT	startTail	Lagtime	ETP	Peak	IPeak	IP-LT	startTail
Enoxaparin Enoxaparin	1,38	1483	286,55	3,48	2,07	14	1,9	1505	226,65	4,75	2,85	18	2,42	1472	184,23	6,31	3,89	20
Enoxaparin Enoxaparin	1,38	1507	303,3	3,2	1,81	15	1,9	1513	252,88	4,49	2,58	17	1,84	1503	182,5	6,05	4,41	18
Mean SD CV %	1,39	1485,00	294,93	3,33	1,94	14,90	1,90	1500,00	220,77	4,82	2,72	17,50	2,03	1487,58	182,42	6,18	4,15	18,00
Mean SD CV %	0,00	31,11	11,84	0,18	0,16	0,71	0,00	5,66	4,41	0,18	0,18	0,71	0,21	21,92	5,02	0,18	0,37	2,63
ration versus not heparinoid added PRP %	-7	-8	-6	-7	-77	-9	-16	-5	-10	-21	-57	-15	-38	-5	-16	-26	-50	-23
WSD3093-Hexasaccharides WSD3093-Hexasaccharides	1,59	1449	285,85	3,48	2,07	14	1,9	1384	202,7	4,75	2,85	17	2,42	1418	175,98	8,05	3,63	21
WSD3093-Hexasaccharides WSD3093-Hexasaccharides	1,38	1387	271,32	3,48	2,07	14	2,16	1404	206,68	4,75	2,58	17	2,68	1433	172,45	6,31	3,63	23
Mean SD CV %	1,39	1418,00	278,59	3,48	2,07	14,90	2,03	1384,00	204,88	4,75	2,72	17,00	2,35	1425,50	174,21	8,18	3,63	22,00
Mean SD CV %	0,00	43,84	10,27	0,00	0,00	0,00	0,00	28,28	2,61	0,00	0,18	0,00	0,18	10,61	2,48	0,18	0,00	1,41
ration versus not heparinoid added PRP %	-7	-12	-11	-3	-75	-13	-10	-13	-13	-2	-67	-17	-22	-9	-7	-26	-56	-5
ration versus Enoxaparin added PRP %	0	-5	-6	-4	-67	-3	-7	-8	-11	-5	-58	-3	-24	-8	-6	-41	-22	-3
WSD3093-Octasaccharides WSD3093-Octasaccharides	1,64	1530	280,91	3,71	2,07	17	2,18	1508	234,48	6	2,84	16	2,98	1510	183,58	6,55	3,87	18
WSD3093-Octasaccharides WSD3093-Octasaccharides	1,38	1497	280,25	3,45	2,07	16	2,16	1543	210,25	6,52	3,38	19	2,68	1512	191,11	6,55	3,87	19
Mean SD CV %	1,51	1513,50	285,53	3,58	2,97	16,50	2,16	1525,50	222,37	5,26	3,10	17,50	2,88	1511,00	182,35	6,55	3,87	18,50
Mean SD CV %	0,18	23,33	6,80	0,18	0,00	0,71	0,00	24,75	17,13	0,57	0,57	2,12	0,00	1,41	1,75	0,00	0,00	0,71
ration versus not heparinoid added PRP %	1	-6	-9	0	-75	3	-4	-4	-6	-63	-15	-18	-4	-18	-21	-53	-20	
ration versus Enoxaparin added PRP %	9	2	-3	3	-67	14	14	1	-14	-50	0	32	2	6	-37	3	-37	
WSD3093-Decasaccharides WSD3093-Decasaccharides	1,38	1517	289,09	3,45	2,07	16	1,75	1483	263,67	4	2,25	15	2,68	1494	204,82	6,65	3,87	19
WSD3093-Decasaccharides WSD3093-Decasaccharides	1,38	1555	282,7	3,71	2,33	21	2,16	1480	216,16	6,26	3,1	18	2,68	1501	201,01	6,3	3,82	21
Mean SD CV %	1,38	1536,00	285,90	3,58	2,20	18,50	1,98	1481,50	255,92	4,83	2,68	15,50	2,88	1511,00	182,35	6,55	3,87	20,00
Mean SD CV %	0,00	26,97	4,52	0,18	0,18	0,64	0,28	2,12	63,38	0,89	0,80	0,00	0,00	12,02	2,65	0,18	0,00	1,41
ration versus not heparinoid added PRP %	-8	-5	-6	0	-74	16	-13	-13	-23	-20	-68	-24	-18	-5	-23	-55	-11	
ration versus Enoxaparin added PRP %	-1	3	-3	8	-64	28	3	-43	11	0	-57	32	0	8	4	-39	11	
WSD3093-Dodecasaccharides WSD3093-Dodecasaccharides	1,64	1685	273,24	3,98	2,34	18	2,42	1608	172,45	6,32	3,8	22	3,2	1704	145,32	8,82	5,72	28
WSD3093-Dodecasaccharides WSD3093-Dodecasaccharides	1,64	1623	278,11	3,98	2,34	18	2,42	1759	177,4	6,32	3,9	23	3,48	1843	138,59	8,43	5,97	27
Mean SD CV %	1,64	1644,00	275,88	3,98	2,34	18,00	2,42	1683,50	174,93	6,32	3,98	22,50	3,33	1673,50	141,98	8,18	5,85	26,50
Mean SD CV %	0,00	28,70	4,52	0,00	0,00	0,00	0,00	106,77	3,50	0,00	0,00	0,71	0,71	43,15	4,76	0,36	0,18	0,71
ration versus not heparinoid added PRP %	9	2	-12	12	-72	13	8	6	-15	9	-53	10	2	6	-13	10	-30	
ration versus Enoxaparin added PRP %	18	-11	-28	20	-62	24	27	12	-32	17	-49	6	-12	-32	-17	14	-47	
WSD3093-Hexadecasaccharides WSD3093-Hexadecasaccharides	1,64	1536	269,76	3,98	2,34	15	2,42	1538	160,08	6,32	3,8	23	3,2	1418	115,65	8,43	6,23	27
WSD3093-Hexadecasaccharides WSD3093-Hexadecasaccharides	1,38	1539	262,11	3,98	2,59	15	2,42	1684	160,69	6,06	3,84	25	3,2	1385	114,14	8,43	6,23	28
Mean SD CV %	1,62	1537,50	280,93	3,98	2,47	15,00	2,42	1551,50	165,39	6,19	3,77	24,98	3,26	1407,98	114,90	8,43	6,23	26,50
Mean SD CV %	0,18	2,12	1,67	0,00	0,16	0,00	0,00	17,66	0,43	0,18	0,18	1,41	0,00	18,97	1,07	0,00	0,00	0,71
ration versus not heparinoid added PRP %	1	-5	-17	12	-70	26	-7	-8	-23	6	-55	17	-2	-11	-29	13	-25	
ration versus Enoxaparin added PRP %	9	4	-12	20	-60	34	27	1	-23	34	-41	49	58	7	-39	53	1	
DIA2844-Hexasaccharides DIA2844-Hexasaccharides	1,68	1631	262,23	4,2	2,32	21	2,4	1531	178,88	6,01	3,61	28	3,17	1559	132,69	8,85	5,68	27
DIA2844-Hexasaccharides DIA2844-Hexasaccharides	1,62	1617	260,45	4,2	2,58	21	2,4	1506	167,28	6,27	3,87	23	3,17	1621	132,69	8,85	5,68	27
Mean SD CV %	1,75	1624,00	258,33	4,20	2,45	18,50	2,40	1519,50	178,08	6,14	3,74	24,58	3,17	1500,00	132,54	8,85	5,68	27,00
Mean SD CV %	0,18	9,80	8,34	0,00	0,18	2,12	0,00	16,26	8,20	0,18	0,18	2,12	0,00	43,84	0,22	0,00	0,00	0
ration versus not heparinoid added PRP %	17	0	-13	18	-71	22	7	4	-17	6	-55	20	-2	1	-19	6	-32	
ration versus Enoxaparin added PRP %	26	-3	-12	16	-62	26	-7	1	-23	33	-41	49	58	7	-39	5	-50	
DIA2844-Octasaccharides DIA2844-Octasaccharides	1,5	1572	267,93	4	2,5	16	2,5	1472	169,86	6,25	3,76	27	3,25	1482	133,68	8,25	5,26	28
DIA2844-Octasaccharides DIA2844-Octasaccharides	1,5	1564	279,92	3,75	2,25	15	2,5	1590	183,14	6	3,6	25	3,15	1559	133,25	8,75	5,26	28
Mean SD CV %	1,50	1568,00	273,93	3,98	2,38	16,00	2,50	1531,00	178,50	6,13	3,63	26,00	3,28	1516,50	133,47	8,50	5,13	28,00
Mean SD CV %	0	0	5,68	8,48	0,18	0,18	0,71	0,00	8,44	9,38	0,36	0,18	0,18	0,18	6,58	0,36	0,18	0,00
ration versus not heparinoid added PRP %	6	-3	-12	9	-71	16	-72	11	-3	-16	5	-56	27	4	-18	2	-38	
ration versus Enoxaparin added PRP %	8	6	-7	16	-62	26	-7	32	1	-23	33	-41	49					

Lagtime	ETP	Peak	tPeak	tP-LT	startTail	Lagtime	ETP	Peak	tPeak	tP-LT	startTail	Lagtime	ETP	Peak	tPeak	tP-LT	startTail
1,5	1637	312,5	3,5	2	16	2,25	1593	204,07	6	3,75	21	3,25	1582	159,26	8,5	5,25	24
1,5	1661	306,63	3,75	2,25	16	2,25	1621	209,88	6	3,75	21	3,25	1592	160,21	8,5	5,25	23
1,5	1638	314,38	3,5	2	16	2,25	1614	210,32	6,75	3,5	20	3,25	1593	175,57	8	4,75	22
1,5	1635	315,7	3,5	2	16	2,25	1517	211,37	5,5	3,25	20	3,25	1523	156,84	8,25	5	24

Mean
SD
CV %

1,50 1817,25 312,77 3,66 2,06 16,00 2,25 1588,25 208,91 5,81 3,56 28,50 3,25 1572,50 162,97 8,31 5,06 23,25

0,00 58,04 3,12 0,13 0,13 0,00 0,00 47,88 3,28 0,24 0,24 0,58 0,00 33,37 8,62 0,24 0,24 0,96

0 3 1 4 6 0 0 3 2 4 7 3 0 2 5 9 5 4

PRP + HEPARINOID 2,5 µg / ml.

Tested molecule	With Hemolysis Recombiplastin 1/40 diluted						With Hemolysis Recombiplastin 1/100 diluted						With Hemolysis Recombiplastin 1/200 diluted					
	Lagtime	ETP	Peak	tPeak	tP-LT	startTail	Lagtime	ETP	Peak	tPeak	tP-LT	startTail	Lagtime	ETP	Peak	tPeak	tP-LT	startTail
Enoxaparin Enoxaparne	1,50	1296	250,57	3,2	1,81	16	1,64	1323	183,26	5,01	3,37	16,14	2,68	1314	150,84	7,35	4,67	24
Enoxaparin	1,55	1647	385,53	3	1,75	16	1,64	1323	173,82	5,01	3,37	16	2,5	1467	225,61	6,25	3,75	20
Mean	1,32	1421,50	307,05	3,10	1,72	17,90	1,84	1323,98	178,44	5,81	3,37	17,87	2,58	130,50	182,83	6,88	4,21	22,00
SD	0,10	177,48	78,87	0,14	0,04	1,41	0,00	0,00	6,91	0,00	0,00	1,32	1,32	100,15	60,79	0,78	0,65	2,83
CV %	7	12	26	5	2	8	0	0	4	0	0	8	6	8	33	11	16	13
ration versus not heparinoid added PRP %	-12	-12	-2	-13	-70	5	-27	-17	-15	-14	-59	-17	-20	-12	-12	-18	-40	-5
WSD3063-Hexasaccharides	1,39	1401	282,74	3,46	2,07	16	2,16	1310	185,23	5,27	3,11	18	2,68	1435	170,85	6,57	3,89	21
WSD3063-Hexasaccharides	1,39	1424	273,41	3,2	1,81	15	1,9	1433	202,18	4,76	2,65	18	2,68	1498	170,63	6,93	4,15	22
Mean	1,39	1412,50	268,98	3,33	1,94	15,50	2,03	1376,00	183,71	5,81	2,98	18,50	2,68	1486,50	170,79	6,70	4,02	21,50
SD	0,00	16,28	7,54	0,18	0,71	0,18	0,00	0,00	6,91	0,37	0,18	0,71	0,00	44,65	0,23	0,18	0,71	3
CV %	0	1	3	6	9	5	9	6	7	6	4	0	3	0	3	5	5	
ration versus not heparinoid added PRP %	-7	-13	-14	-7	-77	-3	-10	-13	-7	-14	-64	-10	-13	-7	-5	-19	-52	-2
ration versus Enoxaparine added PRP %	5	-1	-13	7	-71	-9	-24	-4	-9	-0	-56	-8	-3	-5	-7	-1	-41	-2
WSD3063-Octasaccharides	1,38	1623	276,3	3,45	2,07	17	2,16	1532	203,87	5,62	3,38	18	2,68	1503	162,8	6,81	4,13	20
WSD3063-Octasaccharides	1,38	1621	276,7	3,45	2,07	17	2,16	1538	205,87	5,62	3,38	18	2,94	1620	180,68	7,07	4,13	23
Mean	1,38	1522,00	276,00	3,45	2,07	17,00	2,16	1533,00	204,97	5,62	3,38	19,00	2,94	1511,50	161,79	6,84	4,13	21,50
SD	0,00	14,41	0,98	0,00	0,00	0,00	0,00	4,24	1,41	0,00	0,00	0,18	0,00	22,63	0,76	0,00	0,00	2,12
CV %	0	0	0	0	0	0	0	0	1	0	5	7	0	0	0	0	4	
ration versus not heparinoid added PRP %	-8	-6	-12	-3	-75	6	-4	-3	-2	-5	-50	-7	-14	-4	-12	-17	-50	-8
ration versus Enoxaparine added PRP %	5	7	-10	11	-70	0	32	15	18	10	-51	11	8	9	-1	2	-39	-2
WSD3063-Dodecasaccharides	1,38	1597	280,77	3,71	2,33	17	2,16	1537	203,3	6,62	3,38	20	2,94	1456	182,84	7,07	4,13	19
WSD3063-Dodecasaccharides	1,38	1548	278,75	3,45	2,07	18	1,9	1509	213,47	5,62	3,62	18	2,94	1489	183,91	7,07	4,13	20
Mean	1,38	1572,50	280,26	3,58	2,20	17,50	2,03	1523,00	211,38	6,52	3,49	19,00	2,94	1472,00	183,38	7,07	4,13	19,50
SD	0,00	34,65	0,72	0,18	0,18	0,71	0,18	19,80	2,95	0,00	0,18	1,41	0,00	22,63	0,76	0,00	0,00	0,71
CV %	0	2	0	6	8	4	8	1	0	5	7	0	2	0	0	0	4	
ration versus not heparinoid added PRP %	-8	-3	-10	0	-74	9	-10	-4	1	-5	-58	-7	-10	-6	-13	-15	-50	-11
ration versus Enoxaparine added PRP %	5	11	-9	15	-58	3	24	15	18	10	-49	11	14	6	0	4	-39	-2
WSD3063-Dodecasaccharides	1,64	1483	215,82	4,24	2,6	20	2,16	1472	145,14	6,58	4,42	23	3,48	1413	141,93	6,68	6,75	29
WSD3063-Dodecasaccharides	1,39	1478	223,24	3,98	2,59	18	2,42	1420	120,71	7,38	4,84	28	3,2	1397	118,89	8,17	5,87	27
Mean	1,52	1480,50	219,43	4,11	2,88	19,00	2,42	1386,00	118,43	7,48	5,07	28,60	3,20	1484,50	116,55	9,58	6,36	28,00
SD	0,18	82,23	2,59	0,18	0,01	1,41	0,00	48,08	7,47	0,18	0,18	0,71	0,00	10,61	3,32	0,65	1,41	5
CV %	12	0	2	4	0	7	0	3	6	2	4	2	0	1	3	6	5	
ration versus not heparinoid added PRP %	1	-8	-30	15	-59	19	8	-13	-45	29	-39	39	-2	-11	-28	15	-23	20
ration versus Enoxaparine added PRP %	15	4	-29	33	-52	12	48	-35	50	-25	67	24	1	-36	41	-6	-5	27
WSD3063-Hexadecasaccharides	1,64	1680	229,96	4,24	2,6	20	2,16	1472	145,14	6,58	4,42	23	3,48	1413	109,99	10,21	6,75	32
WSD3063-Hexadecasaccharides	1,39	1582	235,34	4,24	2,65	18	2,16	1435	140,7	6,64	4,68	23	3,48	1413	110,85	9,68	6,49	29
Mean	1,52	1636,00	237,15	4,24	2,73	26,00	2,16	1453,56	142,92	6,71	4,55	23,00	3,33	1613,00	110,42	8,85	8,82	36,50
SD	0,18	82,23	2,56	0,00	0,18	0,00	0,00	26,18	3,14	0,18	0,00	0,18	0,00	0,61	0,37	0,18	2,12	7
CV %	12	4	1	0	6	0	0	2	3	4	6	7	4	1	4	3	7	
ration versus not heparinoid added PRP %	1	1	-24	19	-67	25	-4	-8	-32	15	-45	12	2	-32	20	-2	31	39
ration versus Enoxaparine added PRP %	15	15	-23	37	-60	18	32	10	34	-33	35	29	20	-34	46	-6	-5	39
J6053-->Hexadecasaccharides	1,62	1346	174,7	4,48	2,84	26	2,81	1215	98,71	8,34	5,43	33	4,46	1122	82,16	11,95	7,49	33
J6053-->Hexadecasaccharides	1,62	1314	180,81	4,48	2,84	27	2,81	1203	93,5	8,85	5,94	30	4,42	958	85,87	11,68	7,49	33
Mean	1,62	1330,00	177,76	4,48	2,84	27,50	2,81	1208,00	81,81	8,80	5,89	31,50	4,33	1040,00	74,81	11,82	7,48	33,00
SD	0,00	22,61	4,32	0,00	0,00	0,71	0,00	8,49	2,68	0,36	0,36	2,12	0,18	115,97	11,51	0,18	0,00	0,00
CV %	0	2	2	0	0	3	0	1	3	4	6	7	4	1	2	0	0	
ration versus not heparinoid added PRP %	8	-18	-43	25	-66	72	29	-24	-56	48	-32	54	33	-34	42	-6	42	50
ration versus Enoxaparine added PRP %	23	-6	-42	44	-58	62	77	-6	-30	49	-37	46	17	-32	34	-11	-14	20
DA2844-Hexasaccharides	1,68	1677	243,81	4,72	2,84	18	2,4	1649	168,63	8,63	4,13	24	2,86	1511	127,08	8,85	6,2	23
DA2844-Hexasaccharides	1,62	1626	258,47	4,2	2,58	18	2,4	1616	171,12	8,53	4,13	24	2,86	1511	139,49	9,4	6,95	26
Mean	1,75	1651,00	258,88	4,48	2,71	18,50	2,68	1632,58	168,38	8,63	4,13	25,00	3,04	1475,50	123,83	8,11	6,07	26,50
SD	0,18	56,08	10,56	0,37	0,18	0,71	0,00	23,33	3,88	0,00	0,00	1,41	0,65	50,20	4,46	0,37	0,18	4,66
CV %	11	2	4	8	7	4	0	1	2	0	0	8	3	4	4	1	18	
ration versus not heparinoid added PRP %	17	2	-20	25	-67	16	7	3	-19	12	-50	22	-5	-24	10	-2	-27	14
ration versus Enoxaparine added PRP %	24	16	-13	38	-62	21	19	5</td										

Lagtime	ETP	Peak	tPeak	BP-LT	startTail	Lagtime	ETP	Peak	tPeak	BP-LT	startTail	Lagtime	ETP	Peak	tPeak	BP-LT	startTail
1,5	1637	312,5	3,5	2	16	2,25	1593	204,07	6	3,75	21	3,25	1582	158,26	8,5	5,25	24
1,5	1681	308,53	3,75	2,25	16	2,25	1621	209,86	6	3,75	21	3,25	1592	160,21	8,5	5,25	23
1,5	1636	314,36	3,5	2	16	2,25	1614	210,32	5,75	3,5	20	3,25	1593	175,57	6	4,75	22
1,5	1535	315,7	3,5	2	16	2,25	1617	211,37	5,5	3,25	20	3,25	1523	168,84	8,25	5	24

Mean 1,50 1617,25 312,77 3,56 2,06 16,00 2,25 1586,25 208,91 5,81 3,56 20,50 3,25 1572,50 162,97 8,31 5,06 23,25
SD 0,00 56,04 3,12 0,13 0,13 0,00 0,00 47,68 3,28 0,24 0,24 0,58 0,00 33,37 8,52 0,24 0,24 0,86
CV % 0 3 1 4 6 0 0 3 2 4 7 3 0 2 5 3 5 4

PRP + HEPARINOID 5 µg / ml.

Tested molecule	With Hemoliance Recombiplastin 1/40 diluted						With Hemoliance Recombiplastin 1/100 diluted						With Hemoliance Recombiplastin 1/200 diluted					
	Lagtime	ETP	Peak	tPeak	BP-LT	startTail	Lagtime	ETP	Peak	tPeak	BP-LT	startTail	Lagtime	ETP	Peak	tPeak	BP-LT	startTail
Enoxaparin	1,39	1090	196,46	3,46	2,07	20	2,16	1081	116,66	6,31	4,15	24	3,2	978	77,42	9,84	6,74	26
Enoxaparin	1,38	1067	179,49	3,72	2,33	23	2	1170	220,72	4,75	2,75	16	3,2	967,85	84,47	9,84	6,74	27
Mean	1,39	1078,50	187,98	3,59	2,20	21,50	2,08	1125,50	168,69	5,53	3,45	20,00	3,20	987,93	80,95	9,84	6,74	27,50
SD	0,00	16,26	12,00	0,18	0,18	2,12	0,11	62,93	73,58	1,10	0,89	5,68	0,00	14,04	4,98	0,00	0,00	0,71
CV %	0	2	6	5	8	10	5	6	44	20	29	28	0	1	6	0	0	3
tion versus not heparinoid added PRP %	-7	-33	-40	1	-/4	34	-3	-29	-10	-5	-58	-2	-2	-37	-50	20	-19	12
WSD3093-Hexasaccharides	1,39	1405	258,41	3,46	2,07	16	1,9	1375	182,96	5,27	3,37	18	2,68	1411	152,4	7,09	4,41	21
WSD3093-Hexasaccharides	1,25	1476	349,85	2,76	1,5	14	1,9	1483	193,82	5,27	3,37	19	2,68	1417	151,57	7,09	4,41	24
Mean	1,32	1446,50	364,13	3,11	1,79	15,00	1,90	1434,00	188,39	5,27	3,37	18,50	2,68	1414,00	161,99	7,09	4,41	22,50
SD	0,10	50,20	64,66	0,50	0,40	1,41	0,00	63,44	7,89	0,00	0,00	0,71	0,00	4,24	0,59	0,00	0,00	2,12
CV %	7	3	21	16	23	8	0	6	4	0	4	0	0	0	0	0	0	8
tion versus not heparinoid added PRP %	-12	-11	-3	-13	-79	-6	-16	-10	-10	-9	-59	-10	-18	-10	-15	-47	-47	-3
action versus Enoxaparine added PRP %	-5	-34	62	-14	-82	-30	-27	12	-5	-66	-3	-16	43	-88	-29	-56	-13	-18
WSD3093-Octasaccharides	1,38	1684	249,84	3,97	2,58	20	2,16	1512	178,21	6,55	4,39	20	3,19	1493	168,82	8,11	4,92	24
WSD3093-Octasaccharides	1,64	1651	240,66	4,23	2,58	20	2,16	1535	183,42	6,3	4,14	21	3,19	1496	162,87	7,85	4,66	22
Mean	1,51	1537,50	245,25	4,10	2,59	29,00	2,16	1523,50	189,82	6,43	4,27	20,50	3,19	1494,50	160,85	7,98	4,79	23,00
SD	0,18	8,18	6,48	0,18	0,00	0,00	0,00	16,26	3,68	0,19	0,18	0,71	0,00	2,12	2,98	0,18	0,18	1,41
CV %	12	1	3	4	0	0	1	2	3	4	3	0	0	2	2	4	6	6
tion versus not heparinoid added PRP %	1	-4	-22	15	-62	25	-4	-13	11	-49	0	-2	-5	-1	-4	-42	-1	-1
action versus Enoxaparine added PRP %	9	44	30	14	-74	-7	4	35	7	16	-57	3	0	51	99	-20	-52	-25
WSD3093-Decasaccharides	1,38	1582	260,95	3,87	2,58	17	2,16	1488	182,93	6,3	4,14	21	3,19	1432	157,08	7,85	4,66	22
WSD3093-Decasaccharides	1,38	1512	252,49	3,97	2,58	16	2,16	1530	182,58	6,3	4,14	22	3,19	1489	174,33	7,59	4,65	19
Mean	1,38	1547,00	256,72	3,97	2,58	17,50	2,16	1568,50	182,76	6,30	4,14	21,50	3,07	1465,50	165,76	7,72	4,86	20,50
SD	0,00	46,50	5,98	0,00	0,00	0,71	0,00	28,88	0,25	0,00	0,00	0,71	0,18	47,38	12,21	0,18	0,01	2,12
CV %	0	3	2	0	0	4	0	2	0	0	0	3	6	3	7	2	0	10
tion versus not heparinoid added PRP %	-2	-4	-18	11	-60	9	-4	-5	-13	8	-50	5	-6	-7	2	-7	-44	-12
action versus Enoxaparine added PRP %	-1	43	37	11	-74	-7	4	34	8	14	-58	4	48	105	-22	-53	-25	-18
WSD3093-Dodecasaccharides	1,64	1434	196,26	4,5	2,86	24	2,42	1335	96,91	8,68	6,24	32	3,46	1166	77,83	10,99	7,53	33
WSD3093-Dodecasaccharides	1,39	1560	215,15	4,5	3,11	21	2,42	1439	119,42	7,82	5,2	28	3,46	1086	69,3	11,25	7,79	32
Mean	1,52	1497,00	205,71	4,50	2,99	22,50	2,29	1387,00	108,17	8,14	5,72	30,00	3,46	1126,00	73,57	11,12	7,66	32,50
SD	0,18	69,10	13,36	0,00	0,18	2,12	0,00	73,54	15,92	0,74	0,74	3,23	0,00	65,57	6,03	0,18	0,01	0,71
CV %	12	6	6	0	6	9	0	5	15	9	13	9	0	5	8	2	0	2
tion versus not heparinoid added PRP %	1	-7	-34	26	-64	41	8	-13	-18	46	-31	46	6	-28	34	-8	40	18
action versus Enoxaparine added PRP %	9	39	9	25	-70	5	16	23	-36	47	-42	50	8	14	-9	12	-23	18
WSD3093-Hexadecasaccharides	1,39	1581	203,69	4,5	3,11	22	2,42	1427	119,11	7,38	4,94	27	3,72	1172	80,1	10,88	7,27	33
WSD3093-Hexadecasaccharides	1,64	1548	208,34	4,5	2,86	24	2,16	1422	112,5	7,88	5,72	28	3,46	1235	88,87	10,73	7,27	32
Mean	1,52	1565,00	205,97	4,50	2,89	23,00	2,29	1424,50	119,81	7,82	5,53	27,50	3,58	1203,50	83,49	10,88	7,27	32,50
SD	0,18	22,93	3,36	0,00	0,18	1,41	0,18	3,84	4,67	0,37	0,55	0,71	0,18	44,55	4,79	0,18	0,00	0,71
CV %	12	1	2	0	6	8	0	4	5	10	3	5	4	6	2	0	2	2
tion versus not heparinoid added PRP %	1	-3	-34	26	-64	41	7	-10	-15	31	-38	31	10	-23	-49	31	-13	40
action versus Enoxaparine added PRP %	9	45	10	25	-70	7	10	27	38	-46	33	12	22	3	9	-27	16	18
933->Hexadecasaccharides	1,88	801	82,2	5,24	3,38	29	2,81	526	31,58	11,18	8,27	34	8,27	619	35,67	15,83	9,56	38
933->Hexadecasaccharides	1,62	807	91,38	4,98	3,38	24	3,43	780	57,08	10,4	8,87	33	8,27	632	36,3	15,83	9,56	36
Mean	1,75	804,80	88,79	5,11	3,38	26,50	3,17	652,58	44,34	10,79	7,82	33,50	8,27	825,50	35,99	15,83	9,56	36,00
SD	0,18	4,24	6,48	0,18	0,00	3,64	0,37	180,31	18,02	0,65	0,82	0,71	0,00	8,19	0,45	0,00	0,00	0,00
CV %	11	1	7	4	0	13	12	28	41	5	12	2	0	1	1	0	0	0
tion versus not heparinoid added PRP %	17	-50	-72	43	-60	66	41	-59	86	-8	63	93	-60	-78	00	15	-55	31
action versus Enoxaparine added PRP %	26	-25	-54	42	-66	23	-41	-37	57	-43	23	66	-37	59	-56	59	-34	31
DIA2844-Hexasaccharides	1,62	1718	234,98	4,72	3,1	20	2,4	1821	158,47	6,79	4,39	26	3,69	1632	121,03	10,66	8,87	30
DIA2844-Hexasaccharides	1,62	1708	256,71	4,2	2,68	18	2,4	1844	184,93	6,79	4,39	28	3,43	1571	116,82	10,4	8,87	31
Mean	1,62	1713,50	245,35	4,46	2,84	19,00	2,40	1832,50	168,70	6,79	4,39	25,50	3,68	1601,50	118,98	10,53	8,87	30,50
SD	0,00	7,78	14,68	0,37	0,37	1,41	0,00	16,26	5,89	0,00	0,00	0,71	0,18	43,13	2,91	0,18	0,00	0,71
CV %	0	0	8	6	8	13	7	0	1	4	0	0	3	5	2	0	2	2
tion versus not heparinoid added PRP %	8	6	-22	25	-66	30	24	-59	37	-49	24	22	-7	-24	27	-16	31	11
action versus Enoxaparine added PRP %	17	59	31	24	-71	15	45	-5	-40	43	-33	30	33	-4	-32	31	-21	31
DIA2844-Octasaccharides	1,9	1857	230,52	4,75	2,85	23	2,84	1618	140,54	7,85	4,9							

	Lagtime	ETP	Peak	tPeak	tP-LT	startTall	Lagtime	ETP	Peak	tPeak	tP-LT	startTall	Lagtime	ETP	Peak	tPeak	tP-LT	startTall
	1,5	1637	312,5	3,5	2	16	2,25	1593	204,07	6	3,75	21	3,25	1562	159,26	6,5	6,25	24
	1,5	1661	308,53	3,75	2,25	16	2,25	1621	208,86	6	3,75	21	3,25	1582	160,21	8,5	5,25	23
	1,5	1636	314,36	3,5	2	16	2,25	1614	210,32	5,75	3,6	20	3,25	1593	175,57	8	4,75	22
	1,5	1535	315,7	3,5	2	16	2,25	1517	211,37	5,5	3,25	20	3,25	1523	156,84	8,25	5	24
Mean	1,50	1817,25	312,77	3,56	2,06	16,00	2,25	1586,25	208,91	5,91	3,56	20,50	3,25	1572,50	182,97	8,31	5,06	23,25
SD	0,00	56,04	3,12	0,13	0,13	0,00	0,00	47,68	3,28	0,24	0,24	0,58	0,00	33,37	8,52	0,24	0,24	0,96
CV %	0	3	1	4	6	0	0	3	2	4	7	3	0	2	5	3	5	4
PRP + HEPARINOID 10 ug/ml																		
Tested molecule																		
With Hemoilance Recombiplastin 1/40 diluted																		
Enoxaparine	Lagtime	ETP	Peak	tPeak	tP-LT	startTall	Lagtime	ETP	Peak	tPeak	tP-LT	startTall	Lagtime	ETP	Peak	tPeak	tP-LT	startTall
Enoxaparine	1,30	654	93,89	3,66	2,59	23	2,42	488	32,07	7,8	5,18	31	5,79	466	28,94	13,31	7,52	35
Enoxaparine	1,64	668	83,84	4,49	2,95	27	2,68	431	28,23	8,12	5,44	31	5,63	474	28,44	13,82	6,29	36
Mean	1,32	861,00	88,87	4,24	2,72	25,00	2,55	458,50	36,15	7,86	5,31	31,00	5,86	470,00	29,19	13,57	7,31	35,50
SD	0,18	8,80	7,11	0,36	0,18	2,83	0,18	38,88	2,72	0,37	0,18	0,00	0,18	5,66	1,06	0,36	0,54	0,71
CV %	12	1	8	9	7	11	7	8	9	5	3	0	3	1	4	3	7	2
ration versus not heparinoid added PRP %	1	-59	-72	19	-67	56	13	-71	-86	35	-36	51	74	-70	-82	63	-5	53
WSD3093-Hexasaccharides	1,39	1447	251,22	3,46	2,07	18	1,9	1470	177,7	6,05	4,15	20	2,94	1461	144,3	7,8	4,86	23
WSD3093-Hexasaccharides	1,25	1574	355,06	3	1,75	16	1,9	1450	180,21	5,59	3,63	21	3,2	1993	134,65	8,38	5,18	24
Mean	1,32	1510,50	303,16	3,23	1,91	16,80	1,90	1460,00	178,96	5,78	3,89	28,50	3,07	1427,00	139,43	7,99	4,82	23,50
SD	0,10	89,80	73,45	0,33	0,23	0,00	0,00	14,14	1,77	0,37	0,37	0,71	0,18	48,08	6,88	0,55	0,37	0,71
CV %	12	6	24	10	12	0	0	1	1	6	8	3	6	3	5	7	3	
ration versus not heparinoid added PRP %	-12	-7	-3	-9	-77	0	-16	-8	-14	0	-53	0	-6	-14	-4	-41	-1	
ration versus Enoxaparine added PRP %	-13	129	241	-24	-86	-36	-25	218	404	-25	-71	-34	204	378	-41	-64	-34	
WSD3093-Octasaccharides	1,38	1037	147,78	4,49	3,11	23	2,42	982	100,33	7,33	4,31	23	3,45	938	85,05	9,4	5,95	22
WSD3093-Octasaccharides	1,38	1053	185,76	4,23	2,85	20	2,42	1008	107,88	5,81	4,38	22	3,18	871	86,71	8,62	4,81	22
Mean	1,39	1045,00	158,78	4,38	2,98	21,50	2,42	994,00	104,11	7,87	4,85	22,50	3,58	954,50	91,88	9,01	5,43	23,00
SD	0,00	11,31	12,71	0,18	0,18	2,12	0,00	18,87	5,34	0,37	0,71	0,18	23,33	9,66	0,55	0,74	1,41	
CV %	0	1	8	4	6	10	0	2	5	6	8	3	6	2	6	14	6	
ration versus not heparinoid added PRP %	-8	-35	-50	22	-64	34	8	-37	-50	22	-44	10	-10	-44	8	-35	-1	
ration versus Enoxaparine added PRP %	-9	53	76	3	-78	-14	-5	117	245	-10	-66	-27	103	215	-34	-60	-32	
WSD3093-Decasaccharides	1,64	1461	214,92	4,75	3,11	18	2,42	1386	140,45	7,85	5,43	24	3,71	1264	115,88	9,66	5,85	25
WSD3093-Decasaccharides	1,38	1461	209,28	4,75	3,37	23	2,68	1372	128,86	7,89	4,91	25	3,18	1365	126,06	9,66	6,47	23
Mean	1,51	1461,00	212,18	4,75	3,24	21,00	2,55	1370,00	135,16	7,72	5,17	24,50	3,45	1324,50	120,97	9,88	6,21	24,00
SD	0,18	0,00	3,98	0,00	0,18	2,83	0,18	9,80	7,49	0,18	0,37	0,71	0,57	85,56	7,20	0,00	0,37	1,41
CV %	12	0	2	0	6	13	7	1	6	2	7	3	11	6	6	0	8	
ration versus not heparinoid added PRP %	1	-10	-32	33	-61	31	13	-13	-35	33	-38	20	6	-16	-26	-25	3	
ration versus Enoxaparine added PRP %	0	121	139	12	-76	-16	0	201	348	-2	-62	-21	108	314	-29	-54	-32	
WSD3093-Dodecasaccharides	1,64	1694	165,7	5,64	3,28	28	2,68	1126	71	10,21	7,53	32	5,72	907	57,29	11,25	8,57	33
WSD3093-Dodecasaccharides	1,38	1622	169,91	5,28	3,89	23	2,42	1119	71,45	8,95	7,53	32	5,72	1050	71,93	11,25	7,53	31
Mean	1,52	1552,00	185,56	5,02	3,51	22,50	2,55	1218,50	94,81	9,44	6,89	29,50	3,72	933,50	82,14	11,25	7,53	32,50
SD	0,18	50,91	10,05	0,18	0,01	3,54	0,18	1122,00	71,23	10,08	7,53	32,00	3,72	978,50	64,61	11,77	8,05	32,00
CV %	12	3	6	3	0	14	7	0	0	2	0	0	0	0	10	6	9	
ration versus not heparinoid added PRP %	1	-4	-48	52	-53	59	13	-20	-66	73	-9	56	15	-38	-60	42	-3	
ration versus Enoxaparine added PRP %	0	136	83	28	-71	2	0	145	136	22	-44	3	-34	108	121	-13	-41	-10
WSD3093->Hexadecasaccharides	1,64	1548	185,24	5,02	3,58	23	2,68	1212	92,57	9,95	7,27	30	3,72	917	60,87	11,25	7,53	33
WSD3093->Hexadecasaccharides	1,38	1566	187,75	5,02	3,63	22	2,42	1227	86,65	8,62	6,5	29	3,72	850	63,41	11,25	7,53	32
Mean	1,52	1552,00	185,56	5,02	3,51	22,50	2,55	1218,50	94,81	9,44	6,89	29,50	3,72	933,50	82,14	11,25	7,53	32,50
SD	0,18	5,88	3,19	0,00	0,18	0,71	0,18	10,61	2,98	0,73	0,54	0,71	0,00	23,33	1,80	0,00	0,71	2
CV %	12	0	2	0	5	3	7	1	3	8	2	0	0	0	2	3	0	
ration versus not heparinoid added PRP %	1	-4	-41	41	-53	41	13	-23	-59	62	-17	44	14	-41	-62	35	-8	
ration versus Enoxaparine added PRP %	0	135	109	19	-74	-10	0	166	181	20	-49	-5	-34	89	113	-17	-44	-8
3093-> Hexadecasaccharides	1,75	351	35,81	5,5	3,76	27	5,24	141	7,7	19,18	13,94	37	ND	ND	ND	ND	ND	
3093-> Hexadecasaccharides	1,75	306	39,83	5,25	3,5	17	7,05	272	13,53	23,32	16,27	37	ND	ND	ND	ND	ND	
Mean	1,75	326,50	37,72	5,38	3,63	22,60	8,18	208,50	18,62	21,25	15,11	37,00	ND	ND	ND	ND	ND	
SD	0,00	31,92	2,70	0,18	0,00	7,07	1,26	92,65	4,12	2,83	1,85	0,00	ND	ND	ND	ND	ND	
CV %	0	10	7	3	5	32	21	45	39	14	11	0	0	0	0	2	0	
ration versus not heparinoid added PRP %	17	-80	-88	51	-56	38	173	-87	-85	286	82	80	ND	ND	ND	ND	ND	
ration versus Enoxaparine added PRP %	16	-50	-58	27	-73	-12	141	-55	-65	170	11	19	ND	ND	ND	ND	ND	
DIA2844-Hexasaccharides	1,68	1766	231,1	4,98	3,1	20	2,85	1827	218,77	7,05	4,4	21	4,2	1385	96,65	11,69	7,49	33
DIA2844-Hexasaccharides	1,62	1709	227,71	4,98	3,36	22	2,5	1523	226,47	5	3,85	19	3,85	1433	100,43	11,44	7,49	31
Mean	1,75	1732,50	228,41	4,98	3,23	21,80	2,58	1725,00	222,12	9,53	3,85	20,00	4,48	1409,00	98,49	11,57	7,49	32,00
SD	0,18	33,23	2,40	0,00	0,18	1,41	0,11	286,87	4,74	0,74	0,64	1,41	0,18	33,94	2,74	0,10	0,44	4
CV %	11	2	1	0	6	7	4	17	2	11	16	7	4	2	3	0	4	
ration versus not heparinoid added PRP %	17	7	-27	40	-61	31	14	9	6	12	-52	-2	25	-10	-40	-39	-32	-10
ration versus Enoxaparine added PRP %	16	162	158	18	-76	-16	1	278	837	-17	-71	-35	-28	200	237	-15	-45	-10
DIA2844-Octasaccharides	1,69	1766	208,1	5,62	3,82	25	3,19	1850	184,91	9								

TABLE II

ETP variation % - Hemoliance Recombiplastin 1/100 diluted

		0,25 µg/mL	0,5 µg/mL	1 µg/mL	2,5 µg/mL	5 µg/mL	10 µg/mL
Enoxaparine		-9%	-10%	-5%	-17%	-29%	-71%
Hexasaccharides	WSD3093	-4%	-14%	-13%	-13%	-10%	-8%
	DIA2844	5%	-10%	-4%	3%	3%	9%
Octasaccharides	WSD3093	-1%	4%	-4%	-3%	-4%	-37%
	DIA2844	9%	2%	-3%	5%	2%	3%
Decasaccharides	WSD3093	-6%	-5%	-8%	-4%	-5%	-13%
	DIA2844	6%	5%	-1%	1%	-3%	-16%
Dodecasaccharides	WSD3093	-2%	-1%	6%	-13%	-13%	-29%
	DIA2844	0	7%	9%	2%	-5%	-11%
< Hexadecasaccharides	WSD3093	-8%	-3%	-2%	-8%	-10%	-23%
	DIA2844	6%	8%	5%	2%	8%	-2%
>= Hexadecasaccharides	WSD3093	11%	-1%	-9%	-24%	-59%	-87%
	DIA2844	-10%	-11%	-17%	-39%	-77%	uninterpretable

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TABLE III

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	2,25	1593	204,07	6	3,75	21
	2,25	1621	209,86	6	3,75	21
	2,25	1614	210,32	5,75	3,5	20
	2,25	1517	211,37	5,5	3,25	20
Mean	2,25	1586,25	208,91	5,81	3,56	20,50
SD	0,00	47,68	3,28	0,24	0,24	0,58
CV %	0	3	2	4	7	3
Heparinoid concentration 0,5 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	2,25	1540	166,15	6,25	4	23
Enoxaparine	2,25	1832	166,4	6,25	4	26
Enoxaparine	2,25	1564	172,07	6	3,75	21
Enoxaparine	2,25	1531	171,23	6	3,75	22
Mean	2,25	1616,75	168,96	6,13	3,88	23,00
SD	0,00	144,17	3,12	0,14	0,14	2,16
CV %	0	9	2	2	4	9
Variation versus not heparinoid added PRP %	0	2	-19	5	-33	12
WSD3093->=Hexadecasaccharides	2	1545	246,53	5	3	18
WSD3093->=Hexadecasaccharides	2	1694	243,52	5,25	3,25	24
WSD3093->=Hexadecasaccharides	2	1822	263,68	5	3	20
WSD3093->=Hexadecasaccharides	2	1520	246,67	5	3	18
Mean	2,00	1645,25	250,10	5,06	3,06	20,00
SD	0,00	140,66	9,17	0,13	0,13	2,83
CV %	0	9	4	2	4	14
Variation versus not heparinoid added PRP %	-11	4	20	-13	-14	-2
Variation versus Enoxaparine added PRP %	-11	2	48	-17	-21	-13
DIA2844->=Hexadecasaccharides	2	1649	270,65	4,75	2,75	22
DIA2844->=Hexadecasaccharides	2	1450	257,59	4,5	2,5	16
DIA2844->=Hexadecasaccharides	2	1446	257,51	4,5	2,5	16
DIA2844->=Hexadecasaccharides	2	1409	255,83	4,5	2,5	16
Mean	2,00	1488,50	260,40	4,56	2,56	17,50
SD	0,00	108,58	6,88	0,13	0,13	3,00
CV %	0	7	3	3	5	17
Variation versus not heparinoid added PRP %	-11	-6	25	-22	-28	-15
Variation versus Enoxaparine added PRP %	-11	-8	54	-26	-34	-24

TABLE III

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	2,25	1593	204,07	6	3,75	21
	2,25	1621	209,86	6	3,75	21
	2,25	1614	210,32	5,75	3,5	20
	2,25	1517	211,37	5,5	3,25	20
Mean	2,25	1586,25	208,91	5,81	3,56	20,50
SD	0,00	47,68	3,28	0,24	0,24	0,58
CV %	0	3	2	4	7	3
Heparinoid concentration 1 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	2,25	1647	150,66	6,75	4,5	25
Enoxaparine	2,5	1569	152,25	7	4,5	24
Enoxaparine	2,5	1515	154,52	6,5	4	24
Enoxaparine	2,25	1452	148,8	6,25	4	24
Mean	2,38	1545,75	151,56	6,63	4,25	24,25
SD	0,14	82,72	2,43	0,32	0,29	0,50
CV %	6	5	2	5	7	2
variation versus not heparinoid added PRP %	6	-3	-27	14	-27	18
WSD3093->=Hexadecasaccharides	2	1676	229,27	5,5	3,5	27
WSD3093->=Hexadecasaccharides	2	1457	222,96	5,25	3,25	17
WSD3093->=Hexadecasaccharides	2,25	1573	234,08	5,25	3	20
WSD3093->=Hexadecasaccharides	2,25	1549	230,37	5,25	3	21
Mean	2,13	1563,75	229,17	5,31	3,19	21,25
SD	0,14	90,00	4,62	0,13	0,24	4,19
CV %	7	6	2	2	8	20
variation versus not heparinoid added PRP %	-6	-1	10	-9	-11	4
variation versus Enoxaparine added PRP %	-11	1	51	-20	-25	-12
DIA2844->=Hexadecasaccharides	2	1492	246,98	4,75	2,75	18
DIA2844->=Hexadecasaccharides	2	1436	239,65	4,75	2,75	18
DIA2844->=Hexadecasaccharides	2	1376	233,78	5	3	17
DIA2844->=Hexadecasaccharides	2	1350	233,04	4,75	2,75	17
Mean	2,00	1413,50	238,36	4,81	2,81	17,50
SD	0,00	63,53	6,46	0,13	0,13	0,58
CV %	0	4	3	3	4	3
variation versus not heparinoid added PRP %	-11	-11	14	-17	-21	-15
variation versus Enoxaparine added PRP %	-16	-9	57	-27	-34	-28

TABLE III

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	2,25	1593	204,07	6	3,75	21
	2,25	1621	209,86	6	3,75	21
	2,25	1614	210,32	5,75	3,5	20
	2,25	1517	211,37	5,5	3,25	20
Mean	2,25	1586,25	208,91	5,81	3,56	20,50
SD	0,00	47,68	3,28	0,24	0,24	0,58
CV %	0	3	2	4	7	3
Heparinoid concentration 1,6 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	2,5	1429	135,1	7	4,5	27
Enoxaparine	2,25	1521	146,31	6,75	4,5	24
Enoxaparine	2,25	1539	149,48	7	4,75	26
Enoxaparine	2,25	1436	145,91	6,5	4,25	26
Mean	2,31	1481,25	144,20	6,81	4,50	25,75
SD	0,13	56,84	6,27	0,24	0,20	1,26
CV %	5	4	4	4	5	5
Variation versus not heparinoid added PRP %	3	-7	-31	17	-23	26
WSD3093=>Hexadecasaccharides	2,25	1406	209,59	5,75	3,5	18
WSD3093=>Hexadecasaccharides	2,25	1390	204,43	5,5	3,25	20
WSD3093=>Hexadecasaccharides	2,25	1411	223,51	5,5	3,25	22
WSD3093=>Hexadecasaccharides	2,25	1528	214,03	5,25	3	21
Mean	2,25	1433,75	212,89	5,50	3,25	20,25
SD	0,00	63,47	8,09	0,20	0,20	1,71
CV %	0	4	4	4	6	8
Variation versus not heparinoid added PRP %	0	-10	2	-5	-9	-1
Variation versus Enoxaparine added PRP %	-3	-3	48	-19	-28	-21
DIA2844=>Hexadecasaccharides	2,25	1336	195,66	5,5	3,25	20
DIA2844=>Hexadecasaccharides	2,25	1287	197,74	5,5	3,25	22
DIA2844=>Hexadecasaccharides	2,25	1257	192,32	5,25	3	20
DIA2844=>Hexadecasaccharides	2	1202	202,44	5	3	18
Mean	2,19	1270,50	197,04	5,31	3,13	20,00
SD	0,13	56,09	4,24	0,24	0,14	1,63
CV %	6	4	2	5	5	8
Variation versus not heparinoid added PRP %	-3	-20	-6	-9	-12	-2
Variation versus Enoxaparine added PRP %	-5	-14	37	-22	-31	-22

TABLE III

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	2,25	1593	204,07	6	3,75	21
	2,25	1621	209,86	6	3,75	21
	2,25	1614	210,32	5,75	3,5	20
	2,25	1517	211,37	5,5	3,25	20
Mean	2,25	1586,25	208,91	5,81	3,56	20,50
SD	0,00	47,68	3,28	0,24	0,24	0,58
CV %	0	3	2	4	7	3
Heparinoid concentration 2,5 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	2,5	1368	126,74	7,75	5,25	30
Enoxaparine	2,5	1412	139,59	7,75	5,25	27
Enoxaparine	2,5	1476	128,9	7,75	5,25	27
Enoxaparine	2,5	1315	123,9	6,75	4,25	26
Mean	2,50	1392,75	129,78	7,50	5,00	27,50
SD	0,00	68,21	6,85	0,50	0,50	1,73
CV %	0	5	5	7	10	6
Variation versus not heparinoid added PRP %	11	-12	-38	29	-14	34
WSD3093->=Hexadecasaccharides	2,5	1339	166,65	6,75	4,25	24
WSD3093->=Hexadecasaccharides	2,5	1194	157,13	6,5	4	22
WSD3093->=Hexadecasaccharides	2,75	N.D.	196,27	6,5	3,75	N.D.
WSD3093->=Hexadecasaccharides	2,25	1239	174,58	6	3,75	18
Mean	2,50	1257,33	173,66	6,44	3,94	21,33
SD	0,20	74,22	16,68	0,31	0,24	3,06
CV %	8	6	10	5	6	14
Variation versus not heparinoid added PRP %	11	-21	-17	11	11	4
Variation versus Enoxaparine added PRP %	0	-10	34	-14	-21	-22
DIA2844->=Hexadecasaccharides	2,5	1151	154,23	6,25	3,75	24
DIA2844->=Hexadecasaccharides	2,5	1071	143,32	6,25	3,75	21
DIA2844->=Hexadecasaccharides	2,5	1070	146,45	6	3,5	20
DIA2844->=Hexadecasaccharides	2,25	1010	146,22	5,75	3,5	20
Mean	2,44	1075,50	147,56	6,06	3,63	21,25
SD	0,13	57,85	4,67	0,24	0,14	1,89
CV %	5	5	3	4	4	9
Variation versus not heparinoid added PRP %	8	-32	-29	4	2	4
Variation versus Enoxaparine added PRP %	-3	-23	14	-19	-28	-23

TABLE III

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	2,25	1593	204,07	6	3,75	21
	2,25	1621	209,86	6	3,75	21
	2,25	1614	210,32	5,75	3,5	20
	2,25	1517	211,37	5,5	3,25	20
Mean	2,25	1586,25	208,91	5,81	3,56	20,50
SD	0,00	47,68	3,28	0,24	0,24	0,58
CV %	0	3	2	4	7	3
Heparinoid concentration 4 µg/ml						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	2,75	1285	87,45	9,75	7	35
Enoxaparine	2,75	1219	99,24	8,5	5,75	28
Enoxaparine	2,75	1244	90,37	9	6,25	32
Enoxaparine	2,75	1159	91,33	8,25	5,5	30
Mean	2,75	1226,75	92,10	8,88	6,13	31,25
SD	0,00	52,73	5,04	0,66	0,66	2,99
CV %	0	4	5	7	11	10
Variation versus not heparinoid added PRP %	22	-23	-56	53	5	52
WSD3093=>Hexadecasaccharides	2,75	865	88,19	8,5	5,75	24
WSD3093=>Hexadecasaccharides	2,5	843	89,8	8	5,5	24
WSD3093=>Hexadecasaccharides	2,5	890	96,74	8	5,5	23
WSD3093=>Hexadecasaccharides	2,75	911	103,87	7,75	5	24
Mean	2,63	877,25	94,65	8,06	5,44	23,75
SD	0,14	29,58	7,18	0,31	0,31	0,50
CV %	5	3	8	4	6	2
Variation versus not heparinoid added PRP %	17	-45	-55	39	53	16
Variation versus Enoxaparine added PRP %	-5	-28	3	-9	-11	-24
DIA2844=>Hexadecasaccharides	2,75	714	74,37	7,5	4,75	24
DIA2844=>Hexadecasaccharides	2,5	714	72,08	7,5	5	26
DIA2844=>Hexadecasaccharides	2,75	680	78,49	7	4,25	22
DIA2844=>Hexadecasaccharides	2,75	639	64,3	7,5	4,75	26
Mean	2,69	686,75	72,31	7,38	4,69	24,50
SD	0,13	35,64	5,96	0,25	0,31	1,91
CV %	5	5	8	3	7	8
Variation versus not heparinoid added PRP %	19	-57	-65	27	32	20
Variation versus Enoxaparine added PRP %	-2	-44	-21	-17	-23	-22

TABLE III

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	2,25	1593	204,07	6	3,75	21
	2,25	1621	209,86	6	3,75	21
	2,25	1614	210,32	5,75	3,5	20
	2,25	1517	211,37	5,5	3,25	20
Mean	2,25	1586,25	208,91	5,81	3,56	20,50
SD	0,00	47,68	3,28	0,24	0,24	0,58
CV %	0	3	2	4	7	3
Heparinoid concentration 5 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	3	1048	72,44	9,75	6,75	33
Enoxaparine	3,25	1051	74,65	9,75	6,5	32
Enoxaparine	3	873	66,73	9,5	6,5	32
Enoxaparine	3	968	62,41	10,25	7,25	34
Mean	3,06	985,00	69,06	9,81	6,75	32,75
SD	0,13	83,98	5,55	0,31	0,35	0,96
CV %	4	9	8	3	5	3
Reaction versus not heparinoid added PRP %	36	-38	-67	69	16	60
WSD3093=>Hexadecasaccharides	3	678	56,92	10	7	26
WSD3093=>Hexadecasaccharides	2,75	624	55,74	9,25	6,5	29
WSD3093=>Hexadecasaccharides	3	695	57,71	9,5	6,5	27
WSD3093=>Hexadecasaccharides	3	688	55,18	9,75	6,75	28
Mean	2,94	671,25	56,39	9,63	6,69	27,50
SD	0,13	32,26	1,14	0,32	0,24	1,29
CV %	4	5	2	3	4	5
Reaction versus not heparinoid added PRP %	31	-58	-73	66	88	34
Reaction versus Enoxaparine added PRP %	-4	-32	-18	-2	-1	-16
DIA2844=>Hexadecasaccharides	3	535	46,99	8,25	5,25	29
DIA2844=>Hexadecasaccharides	3	515	44,31	8,25	5,25	30
DIA2844=>Hexadecasaccharides	3,25	501	41,78	8,75	5,5	31
DIA2844=>Hexadecasaccharides	2,75	505	44,93	7,75	5	28
Mean	3,00	514,00	44,50	8,25	5,25	29,50
SD	0,20	15,19	2,15	0,41	0,20	1,29
CV %	7	3	5	5	4	4
Reaction versus not heparinoid added PRP %	33	-68	-79	42	47	44
Reaction versus Enoxaparine added PRP %	-2	-48	-36	-16	-22	-10

TABLE III

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	2,25	1593	204,07	6	3,75	21
	2,25	1621	209,86	6	3,75	21
	2,25	1614	210,32	5,75	3,5	20
	2,25	1517	211,37	5,5	3,25	20
Mean	2,25	1586,25	208,91	5,81	3,56	20,50
SD	0,00	47,68	3,28	0,24	0,24	0,58
CV %	0	3	2	4	7	3
Heparinoid concentration 6,25 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	3	737	43,43	11,25	8,25	34
Enoxaparine	3	796	50,36	10,25	7,25	34
Enoxaparine	3	832	53,97	9,75	6,75	34
Enoxaparine	3	806	48,54	11	8	35
Mean	3,00	792,75	49,08	10,56	7,56	34,25
SD	0,00	40,14	4,39	0,69	0,69	0,50
CV %	0	5	9	7	9	1
variation versus not heparinoid added PRP %	33	-50	-77	82	30	67
WSD3093->=Hexadecasaccharides	2,75	492	33,99	10,25	7,5	30
WSD3093->=Hexadecasaccharides	2,75	465	32,33	10,25	7,5	31
WSD3093->=Hexadecasaccharides	3	532	37,81	10,25	7,25	30
WSD3093->=Hexadecasaccharides	2,75	489	34,72	10,25	7,5	30
Mean	2,81	494,50	34,71	10,25	7,44	30,25
SD	0,13	27,77	2,29	0,00	0,13	0,50
CV %	4	6	7	0	2	2
variation versus not heparinoid added PRP %	25	-69	-83	76	109	48
/variation versus Enoxaparine added PRP %	-6	-38	-29	-3	-2	-12
DIA2844->=Hexadecasaccharides	3,25	353	26,52	10,75	7,5	29
DIA2844->=Hexadecasaccharides	3	320	23,01	9,25	6,25	32
DIA2844->=Hexadecasaccharides	3	347	25,66	9,75	6,75	30
DIA2844->=Hexadecasaccharides	3	344	25,51	9,5	6,5	31
Mean	3,06	341,00	25,18	9,81	6,75	30,50
SD	0,13	14,49	1,51	0,66	0,54	1,29
CV %	4	4	6	7	8	4
variation versus not heparinoid added PRP %	36	-79	-88	69	89	49
/variation versus Enoxaparine added PRP %	2	-57	-49	-7	-11	-11

TABLE III

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	2,25	1593	204,07	6	3,75	21
	2,25	1621	209,86	6	3,75	21
	2,25	1614	210,32	5,75	3,5	20
	2,25	1517	211,37	5,5	3,25	20
Mean	2,25	1586,25	208,91	5,81	3,56	20,50
SD	0,00	47,68	3,28	0,24	0,24	0,58
CV %	0	3	2	4	7	3
Heparinoid concentration 8 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	3,75	615	37,03	11,75	8	35
Enoxaparine	3,25	483	29,1	11,5	8,25	33
Enoxaparine	3,5	520	29,52	12	8,5	34
Enoxaparine	3,75	685	37,82	11,25	7,5	32
Mean	3,56	575,75	33,37	11,63	8,06	33,50
SD	0,24	91,63	4,70	0,32	0,43	1,29
CV %	7	16	14	3	5	4
Variation versus not heparinoid added PRP %	58	-64	-84	100	39	63
WSD3093->=Hexadecasaccharides	3,5	223	14,74	11,75	8,25	31
WSD3093->=Hexadecasaccharides	3	282	17,76	10,25	7,25	31
WSD3093->=Hexadecasaccharides	3	295	17,89	10,5	7,5	32
WSD3093->=Hexadecasaccharides	3	269	17,26	10	7	32
Mean	3,13	267,25	16,91	10,63	7,50	31,50
SD	0,25	31,35	1,47	0,78	0,54	0,58
CV %	8	12	9	7	7	2
Variation versus not heparinoid added PRP %	39	-83	-92	83	111	54
Variation versus Enoxaparine added PRP %	-12	-54	-49	-9	-7	-6
DIA2844->=Hexadecasaccharides	3,25	204	14,41	10,25	7	30
DIA2844->=Hexadecasaccharides	3,75	189	13,68	10,25	6,5	29
DIA2844->=Hexadecasaccharides	3	168	11,68	10,5	7,5	29
DIA2844->=Hexadecasaccharides	4	235	16,74	11,25	7,25	32
Mean	3,50	199,00	14,13	10,56	7,06	30,00
SD	0,46	28,18	2,09	0,47	0,43	1,41
CV %	13	14	15	4	6	5
Variation versus not heparinoid added PRP %	56	-87	-93	82	98	46
Variation versus Enoxaparine added PRP %	-2	-65	-58	-9	-12	-10

TABLE III

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	2,25	1593	204,07	6	3,75	21
	2,25	1621	209,86	6	3,75	21
	2,25	1614	210,32	5,75	3,5	20
	2,25	1517	211,37	5,5	3,25	20
Mean	2,25	1586,25	208,91	5,81	3,56	20,50
SD	0,00	47,68	3,28	0,24	0,24	0,58
CV %	0	3	2	4	7	3
Heparinoid concentration 9 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	4,25	382	23,24	14,75	10,5	26
Enoxaparine	4	353	20,3	13,75	9,75	33
Enoxaparine	3,75	391	22,48	12,25	8,5	33
Enoxaparine	3,75	390	22,9	11,75	8	33
Mean	3,94	379,00	22,23	13,13	9,19	31,25
SD	0,24	17,80	1,32	1,38	1,14	3,50
CV %	6	5	6	10	12	11
Variation versus not heparinoid added PRP %	75	-76	-39	126	58	52
WSD3093->=Hexadecasaccharides	3,25	223	13,65	11,25	8	32
WSD3093->=Hexadecasaccharides	3,25	184	10,64	10,75	7,5	32
WSD3093->=Hexadecasaccharides	3	206	12,47	11,25	8,25	32
WSD3093->=Hexadecasaccharides	3	187	11,8	10,5	7,5	30
Mean	3,13	200,00	12,14	10,94	7,81	31,50
SD	0,14	18,17	1,26	0,38	0,38	1,00
CV %	5	9	10	3	5	3
Variation versus not heparinoid added PRP %	39	-87	-94	88	119	54
Variation versus Enoxaparine added PRP %	-21	-47	-45	-17	-15	1
DIA2844->=Hexadecasaccharides	4	144	8,86	13,5	9,5	32
DIA2844->=Hexadecasaccharides	4,75	148	9,91	12,5	7,75	30
DIA2844->=Hexadecasaccharides	4	140	9,82	11,5	7,5	30
DIA2844->=Hexadecasaccharides	2,5	124	8,36	11,5	9	30
Mean	3,81	139,00	9,24	12,25	8,44	30,50
SD	0,94	10,52	0,75	0,96	0,97	1,00
CV %	25	8	8	8	11	3
Variation versus not heparinoid added PRP %	69	-91	-96	111	137	49
Variation versus Enoxaparine added PRP %	-3	-63	-58	-7	-8	-2

TABLE III

Without Heparinoid					
With Hemoliance Recombiplastin 1/100 diluted					
Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
2,25	1593	204,07	6	3,75	21
2,25	1621	209,86	6	3,75	21
2,25	1614	210,32	5,75	3,5	20
2,25	1517	211,37	5,5	3,25	20

Mean	2,25	1586,25	208,91	5,81	3,56	20,50
SD	0,00	47,68	3,28	0,24	0,24	0,58
CV %	0	3	2	4	7	3

Tested molecule	Heparinoid concentration 10 µg/mL					
	With Hemoliance Recombiplastin 1/100 diluted					
Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail	
Enoxaparine	4,75	353	21	13,75	9	33
Enoxaparine	4,5	376	22,9	13,25	8,75	33
Enoxaparine	4,75	273	16,57	12,75	8	31
Enoxaparine	3,5	215	11,98	13	9,5	32
Mean	4,38	304,25	18,11	13,19	8,81	32,25
SD	0,60	74,09	4,87	0,43	0,63	0,96
CV %	14	24	27	3	7	3
Variation versus not heparinoid added PRP %	94	-81	-91	127	52	57
WSD3093->=Hexadecasaccharides	3,75	142	8,73	11,5	7,75	31
WSD3093->=Hexadecasaccharides	4,5	99	5,28	15	10,5	33
WSD3093->=Hexadecasaccharides	3	109	6,7	11,25	8,25	31
WSD3093->=Hexadecasaccharides	3,25	120	6,35	11,75	8,5	30
Mean	3,63	117,50	6,77	12,38	8,75	31,25
SD	0,66	18,45	1,44	1,76	1,21	1,26
CV %	18	16	21	14	14	4
Variation versus not heparinoid added PRP %	61	-93	-97	113	146	52
Variation versus Enoxaparine added PRP %	-17	-61	-63	-6	-1	-3
DIA2844->=Hexadecasaccharides	4,5	157	8,33	18	13,5	34
DIA2844->=Hexadecasaccharides	5	142	8,23	17,25	12,25	34
DIA2844->=Hexadecasaccharides	4,75	138	7,4	16	11,25	33
DIA2844->=Hexadecasaccharides	3	93	5,53	13	10	30
Mean	4,31	132,50	7,37	16,06	11,75	32,75
SD	0,90	27,57	1,30	2,20	1,49	1,89
CV %	21	21	18	14	13	6
Variation versus not heparinoid added PRP %	92	-92	-96	176	230	60
Variation versus Enoxaparine added PRP %	-1	-56	-59	22	33	2

TABLE IV

Without Heparinoid					
With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT
	1,75	1322	182,78	4,5	2,75
	1,75	1300	203,28	4,25	2,5
	1,75	1278	197,72	4,25	2,5
	1,75	1140	188,99	4	2,25
Mean	1,75	1260,00	193,19	4,25	2,50
SD	0,00	81,99	9,10	0,20	0,20
CV %	0	7	5	5	8
Heparinoid concentration 0,5 µg/mL					
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted				
	Lagtime	ETP	Peak	ttPeak	ttP - LT
Enoxaparine	1,75	1258	199,92	4,25	2,5
Enoxaparine	1,75	1308	196,03	4,25	2,5
Enoxaparine	1,75	1206	185,78	4,5	2,75
Mean	1,75	1257,33	193,91	4,33	2,58
SD	0,00	51,00	7,30	0,14	0,14
CV %	0	4	4	3	6
Variation versus not heparinoid added PRP %	0	0	0	2	-39
WSD3093->=Hexadecasaccharides	1,75	1511	237	4,25	2,5
WSD3093->=Hexadecasaccharides	1,75	1332	225,02	4,25	2,5
WSD3093->=Hexadecasaccharides	1,75	1367	231,27	4,25	2,5
Mean	1,75	1403,33	231,10	4,25	2,50
SD	0,00	94,87	5,99	0,00	0,00
CV %	0	7	3	0	0
Variation versus not heparinoid added PRP %	0	11	20	0	8
Variation versus Enoxaparine added PRP %	0	12	19	-2	-3
DIA2844->=Hexadecasaccharides	1,75	1430	242,97	4,25	2,5
DIA2844->=Hexadecasaccharides	1,75	1413	236,18	4,25	2,5
DIA2844->=Hexadecasaccharides	1,75	1396	253,04	4,25	2,5
Mean	1,75	1413,00	244,06	4,25	2,50
SD	0,00	17,00	8,48	0,00	0,00
CV %	0	1	3	0	0
Variation versus not heparinoid added PRP %	0	12	26	0	0
Variation versus Enoxaparine added PRP %	0	12	26	-2	-3

TABLE IV

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	1,75	1322	182,78	4,5	2,75	27
	1,75	1300	203,28	4,25	2,5	17
	1,75	1278	197,72	4,25	2,5	17
	1,75	1140	188,99	4	2,25	17
Mean	1,75	1260,00	193,19	4,25	2,50	19,50
SD	0,00	81,99	9,10	0,20	0,20	5,00
CV %	0	7	5	5	8	26
Heparinoid concentration 1 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	1,75	1244	185,15	4,25	2,5	19
Enoxaparine	1,75	1195	187,74	4,5	2,75	18
Enoxaparine	1,75	1448	197,97	4,5	2,75	24
Mean	1,75	1295,67	190,29	4,42	2,67	20,33
SD	0,00	134,18	6,78	0,14	0,14	3,21
CV %	0	10	4	3	5	16
Variation versus not heparinoid added PRP %	0	3	-2	4	-37	4
WSD3093->=Hexadecasaccharides	1,75	1338	224,83	4,25	2,5	19
WSD3093->=Hexadecasaccharides	1,75	1331	217,57	4,5	2,75	21
WSD3093->=Hexadecasaccharides	1,75	1313	222,82	4,5	2,75	20
Mean	1,75	1327,33	221,74	4,42	2,67	20,00
SD	0,00	12,90	3,75	0,14	0,14	1,00
CV %	0	1	2	3	5	5
Variation versus not heparinoid added PRP %	0	5	15	4	7	3
Variation versus Enoxaparine added PRP %	0	2	17	0	0	-2
DIA2844->=Hexadecasaccharides	1,75	1387	232,59	4,5	2,75	18
DIA2844->=Hexadecasaccharides	1,75	1292	219,46	4,5	2,75	17
DIA2844->=Hexadecasaccharides	1,75	1306	212,89	4,5	2,75	24
Mean	1,75	1328,33	221,65	4,50	2,75	19,67
SD	0,00	51,29	10,03	0,00	0,00	3,79
CV %	0	4	5	0	0	19
Variation versus not heparinoid added PRP %	0	5	15	6	10	1
Variation versus Enoxaparine added PRP %	0	3	16	2	3	-3

TABLE IV

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	1,75	1322	182,78	4,5	2,75	27
	1,75	1300	203,28	4,25	2,5	17
	1,75	1278	197,72	4,25	2,5	17
	1,75	1140	188,99	4	2,25	17
Mean	1,75	1260,00	193,19	4,25	2,50	19,50
SD	0,00	81,99	9,10	0,20	0,20	5,00
CV %	0	7	5	5	8	26
Heparinoid concentration 1,6 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	2	1185	169,39	4,75	2,75	19
Enoxaparine	2	ND	186,49	4,75	2,75	ND
Enoxaparine	1,75	1255	177,46	4,5	2,75	25
Mean	1,92	1220,00	177,78	4,67	2,75	22,00
SD	0,14	49,50	8,55	0,14	0,00	4,24
CV %	8	4	5	3	0	19
Variation versus not heparinoid added PRP %	10	-3	-8	10	-35	13
WSD3093->=Hexadecasaccharides	1,75	1229	202,04	4,75	3	24
WSD3093->=Hexadecasaccharides	2	1213	198,39	4,75	2,75	22
WSD3093->=Hexadecasaccharides	2	1233	199,33	4,5	2,5	21
Mean	1,92	1225,00	199,92	4,67	2,75	22,33
SD	0,14	10,58	1,90	0,14	0,25	1,53
CV %	8	1	1	3	9	7
Variation versus not heparinoid added PRP %	10	-3	3	10	10	15
Variation versus Enoxaparine added PRP %	0	0	12	0	0	2
DIA2844->=Hexadecasaccharides	2	1306	196,43	5	3	24
DIA2844->=Hexadecasaccharides	2	1153	186,35	4,75	2,75	25
DIA2844->=Hexadecasaccharides	2	1242	182,26	5	3	26
Mean	2,00	1233,67	188,35	4,92	2,92	25,00
SD	0,00	76,84	7,29	0,14	0,14	1,00
CV %	0	6	4	3	5	4
Variation versus not heparinoid added PRP %	14	-2	-3	16	17	28
Variation versus Enoxaparine added PRP %	4	1	6	5	6	14

TABLE IV

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	1,75	1322	182,78	4,5	2,75	27
	1,75	1300	203,28	4,25	2,5	17
	1,75	1278	197,72	4,25	2,5	17
	1,75	1140	188,99	4	2,25	17
Mean	1,75	1260,00	193,19	4,25	2,50	19,50
SD	0,00	81,99	9,10	0,20	0,20	5,00
CV %	0	7	5	5	8	26
Heparinoid concentration 2,5 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	2	1205	156,13	5,25	3,25	20
Enoxaparine	2,25	1183	150,26	5,5	3,25	21
Enoxaparine	2	1089	147,19	5	3	20
Mean	2,08	1159,00	151,19	5,25	3,17	20,33
SD	0,14	61,61	4,54	0,25	0,14	0,58
CV %	7	5	3	5	5	3
Variation versus not heparinoid added PRP %	19	-8	-22	24	-25	4
WSD3093->=Hexadecasaccharides	2	1091	164,66	5,25	3,25	22
WSD3093->=Hexadecasaccharides	2	1069	158,65	5,5	3,5	20
WSD3093->=Hexadecasaccharides	2	1070	163,16	5,25	3,25	22
Mean	2,00	1076,67	162,16	5,33	3,33	21,33
SD	0,00	12,42	3,13	0,14	0,14	1,15
CV %	0	1	2	3	4	5
Variation versus not heparinoid added PRP %	14	-15	-16	25	33	9
Variation versus Enoxaparine added PRP %	-4	-7	7	2	5	5
DIA2844->=Hexadecasaccharides	2,25	970	141,78	5,75	3,5	22
DIA2844->=Hexadecasaccharides	2,25	964	139,78	5,5	3,25	25
DIA2844->=Hexadecasaccharides	2	912	133,24	5,5	3,5	21
Mean	2,17	948,67	138,27	5,58	3,42	22,67
SD	0,14	31,90	4,47	0,14	0,14	2,08
CV %	7	3	3	3	4	9
Variation versus not heparinoid added PRP %	24	-25	-28	31	37	16
Variation versus Enoxaparine added PRP %	4	-18	-9	6	8	11

TABLE IV

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	1,75	1322	182,78	4,5	2,75	27
	1,75	1300	203,28	4,25	2,5	17
	1,75	1278	197,72	4,25	2,5	17
	1,75	1140	188,99	4	2,25	17
Mean	1,75	1260,00	193,19	4,25	2,50	19,50
SD	0,00	81,99	9,10	0,20	0,20	5,00
CV %	0	7	5	5	8	26
Heparinoid concentration 4 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	2,25	1031	117,98	5,75	3,5	24
Enoxaparine	2,25	1063	131,14	5,75	3,5	20
Enoxaparine	2,5	1047	116,58	6	3,5	23
Mean	2,33	1047,00	121,90	5,83	3,50	22,33
SD	0,14	16,00	8,03	0,14	0,00	2,08
CV %	6	2	7	2	0	9
Variation versus not heparinoid added PRP %	33	-17	-37	37	-18	15
WSD3093->=Hexadecasaccharides	2,25	720	94,69	6,5	4,25	24
WSD3093->=Hexadecasaccharides	2,5	712	94,17	6,5	4	20
WSD3093->=Hexadecasaccharides	2,25	698	93,22	6,25	4	21
Mean	2,33	710,00	94,03	6,42	4,08	21,67
SD	0,14	11,14	0,75	0,14	0,14	2,08
CV %	6	2	1	2	4	10
Variation versus not heparinoid added PRP %	33	-44	-51	51	63	11
Variation versus Enoxaparine added PRP %	0	-32	-23	10	17	-3
DIA2844->=Hexadecasaccharides	2,5	624	78,73	7	4,5	18
DIA2844->=Hexadecasaccharides	2,5	559	68,62	7	4,5	20
DIA2844->=Hexadecasaccharides	2,5	584	65,13	7	4,5	24
Mean	2,50	589,00	70,83	7,00	4,50	20,67
SD	0,00	32,79	7,06	0,00	0,00	3,06
CV %	0	6	10	0	0	15
Variation versus not heparinoid added PRP %	43	-53	-63	65	80	6
Variation versus Enoxaparine added PRP %	7	-44	-42	20	29	-7

TABLE IV

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	1,75	1322	182,78	4,5	2,75	27
	1,75	1300	203,28	4,25	2,5	17
	1,75	1278	197,72	4,25	2,5	17
	1,75	1140	188,99	4	2,25	17
Mean	1,75	1260,00	193,19	4,25	2,50	19,50
SD	0,00	81,99	9,10	0,20	0,20	5,00
CV %	0	7	5	5	8	26
Heparinoid concentration 5 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	2,5	1006	103,76	6,75	4,25	24
Enoxaparine	2,5	844	102,14	6,25	3,75	15
Enoxaparine	2,5	963	109,58	6	3,5	22
Mean	2,50	937,67	105,16	6,33	3,83	20,33
SD	0,00	83,92	3,91	0,38	0,38	4,73
CV %	0	9	4	6	10	23
variation versus not heparinoid added PRP %	43	-26	-46	49	-10	4
WSD3093=>Hexadecasaccharides	2,5	578	71,84	6,5	4	22
WSD3093=>Hexadecasaccharides	2,25	543	71,22	6,5	4,25	18
WSD3093=>Hexadecasaccharides	2,5	558	72,21	6,25	3,75	20
Mean	2,42	559,67	71,76	6,42	4,00	20,00
SD	0,14	17,56	0,50	0,14	0,25	2,00
CV %	6	3	1	2	6	10
variation versus not heparinoid added PRP %	38	-56	-63	51	60	3
variation versus Enoxaparine added PRP %	-3	-40	-32	1	4	-2
DIA2844=>Hexadecasaccharides	2,5	458	49,88	7,5	5	22
DIA2844=>Hexadecasaccharides	2,5	426	45,08	7,75	5,25	22
DIA2844=>Hexadecasaccharides	2,5	420	46,37	7,25	4,75	22
Mean	2,50	434,67	47,11	7,50	5,00	22,00
SD	0,00	20,43	2,48	0,25	0,25	0,00
CV %	0	5	5	3	5	0
variation versus not heparinoid added PRP %	43	-66	-76	76	100	13
variation versus Enoxaparine added PRP %	0	-54	-55	18	30	8

► TABLE IV

	Without Heparinoid					
	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
1,75	1322	182,78	4,5	2,75	27	
1,75	1300	203,28	4,25	2,5	17	
1,75	1278	197,72	4,25	2,5	17	
1,75	1140	188,99	4	2,25	17	
Mean	1,75	1260,00	193,19	4,25	2,50	19,50
SD	0,00	81,99	9,10	0,20	0,20	5,00
CV %	0	7	5	5	8	26
Heparinoid concentration 6,25 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	2,75	853	73,94	7,25	4,5	30
Enoxaparine	2,75	709	66,4	7	4,25	26
Enoxaparine	3	ND	81,98	7,5	4,5	ND
Mean	2,83	781,00	74,11	7,25	4,42	28,00
SD	0,14	101,82	7,79	0,25	0,14	2,83
CV %	5	13	11	3	3	10
Variation versus not heparinoid added PRP %	62	-38	-62	71	4	44
WSD3093->=Hexadecasaccharides	2,75	492	51,2	7,75	5	24
WSD3093->=Hexadecasaccharides	2,5	443	47,31	7,5	5	22
WSD3093->=Hexadecasaccharides	2,75	476	52,88	7	4,25	20
Mean	2,67	470,33	50,46	7,42	4,75	22,00
SD	0,14	24,99	2,86	0,38	0,43	2,00
CV %	5	5	6	5	9	9
Variation versus not heparinoid added PRP %	52	-63	-74	75	90	13
Variation versus Enoxaparine added PRP %	-6	-40	-32	2	8	-21
DIA2844->=Hexadecasaccharides	3	355	30,8	8,5	5,5	25
DIA2844->=Hexadecasaccharides	3	351	30,37	8,5	5,5	27
DIA2844->=Hexadecasaccharides	2,75	328	26,37	8,75	6	27
Mean	2,92	344,67	29,18	8,58	5,67	26,33
SD	0,14	14,57	2,44	0,14	0,29	1,15
CV %	5	4	8	2	5	4
Variation versus not heparinoid added PRP %	67	-73	-85	102	127	35
Variation versus Enoxaparine added PRP %	3	-56	-61	18	28	-6

TABLE IV

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	1,75	1322	182,78	4,5	2,75	27
	1,75	1300	203,28	4,25	2,5	17
	1,75	1278	197,72	4,25	2,5	17
	1,75	1140	188,99	4	2,25	17
Mean	1,75	1260,00	193,19	4,25	2,50	19,50
SD	0,00	81,99	9,10	0,20	0,20	5,00
CV %	0	7	5	5	8	26
Heparinoid concentration 8 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	3	563	48,52	8	5	28
Enoxaparine	3	713	52,78	8,25	5,25	34
Enoxaparine	3	642	49,26	8	5	31
Mean	3,00	639,33	50,19	8,08	5,08	31,00
SD	0,00	75,04	2,28	0,14	0,14	3,00
CV %	0	12	5	2	3	10
Variation versus not heparinoid added PRP %	71	-49	-74	90	20	59
WSD3093->=Hexadecasaccharides	2,75	329	26,84	7,75	5	27
WSD3093->=Hexadecasaccharides	2,75	339	27,51	8,75	6	28
WSD3093->=Hexadecasaccharides	3	365	27,82	8,5	5,5	31
Mean	2,83	344,33	27,39	8,33	5,50	28,67
SD	0,14	18,58	0,50	0,52	0,50	2,08
CV %	5	5	2	6	9	7
Variation versus not heparinoid added PRP %	62	-73	-86	96	120	47
Variation versus Enoxaparine added PRP %	-6	-46	-45	3	8	-8
DIA2844->=Hexadecasaccharides	3	244	17,15	9,5	6,5	32
DIA2844->=Hexadecasaccharides	3,25	239	16,74	10	6,75	30
DIA2844->=Hexadecasaccharides	3,25	225	16,45	9,25	6	29
Mean	3,17	236,00	16,78	9,58	6,42	30,33
SD	0,14	9,85	0,35	0,38	0,38	1,53
CV %	5	4	2	4	6	5
Variation versus not heparinoid added PRP %	81	-31	-91	125	157	56
Variation versus Enoxaparine added PRP %	6	-63	-67	19	26	-2

TABLE IV

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	1,75	1322	182,78	4,5	2,75	27
	1,75	1300	203,28	4,25	2,5	17
	1,75	1278	197,72	4,25	2,5	17
	1,75	1140	188,99	4	2,25	17
Mean	1,75	1260,00	193,19	4,25	2,50	19,50
SD	0,00	81,99	9,10	0,20	0,20	5,00
CV %	0	7	5	5	8	26
Heparinoid concentration 9 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	3,25	540	34,11	9,5	6,25	34
Enoxaparine	3,25	584	38,2	8,5	5,25	33
Enoxaparine	3,25	508	35,44	8,5	5,25	32
Mean	3,25	544,00	35,92	8,83	5,58	33,00
SD	0,00	38,16	2,09	0,58	0,58	1,00
CV %	0	7	6	7	10	3
Variation versus not heparinoid added PRP %	86	-57	-81	108	31	69
WSD3093->=Hexadecasaccharides	3,25	299	23,08	7,75	4,5	29
WSD3093->=Hexadecasaccharides	3	278	21,24	10	7	27
WSD3093->=Hexadecasaccharides	3,5	283	20,49	9,25	5,75	30
Mean	3,25	286,67	21,60	9,00	5,75	28,67
SD	0,25	10,97	1,33	1,15	1,25	1,53
CV %	8	4	6	13	22	5
Variation versus not heparinoid added PRP %	86	-77	-89	112	130	47
Variation versus Enoxaparine added PRP %	0	-47	-40	2	3	-13
DIA2844->=Hexadecasaccharides	3,25	208	15,66	10,25	7	31
DIA2844->=Hexadecasaccharides	3,5	168	11,45	9,5	6	31
DIA2844->=Hexadecasaccharides	3,25	166	12,57	8,75	5,5	29
Mean	3,33	180,67	13,23	9,50	6,17	30,33
SD	0,14	23,69	2,18	0,75	0,76	1,15
CV %	4	13	16	8	12	4
Variation versus not heparinoid added PRP %	90	-86	-93	124	147	56
Variation versus Enoxaparine added PRP %	3	-67	-63	3	10	-8

TABLE IV

Without Heparinoid						
With Hemoliance Recombiplastin 1/100 diluted						
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
	1,75	1322	182,78	4,5	2,75	27
	1,75	1300	203,28	4,25	2,5	17
	1,75	1278	197,72	4,25	2,5	17
	1,75	1140	188,99	4	2,25	17
Mean	1,75	1260,00	193,19	4,25	2,50	19,50
SD	0,00	81,99	9,10	0,20	0,20	5,00
CV %	0	7	5	5	8	26
Heparinoid concentration 10 µg/mL						
Tested molecule	With Hemoliance Recombiplastin 1/100 diluted					
	Lagtime	ETP	Peak	ttPeak	ttP - LT	startTail
Enoxaparine	4	480	34,61	12,25	8,25	33
Enoxaparine	3,75	430	27,29	10,5	6,75	33
Enoxaparine	3,75	456	34,3	8,75	5	30
Mean	3,83	455,33	32,07	10,50	6,67	32,00
SD	0,14	25,01	4,14	1,75	1,63	1,73
CV %	4	5	13	17	24	5
Variation versus not heparinoid added PRP %	119	-64	-83	147	57	64
WSD3093->=Hexadecasaccharides	3,5	248	17,16	9,5	6	31
WSD3093->=Hexadecasaccharides	3,5	186	12,5	10	6,5	32
WSD3093->=Hexadecasaccharides	3,5	215	13,81	10,25	6,75	34
Mean	3,50	216,33	14,49	9,92	6,42	32,33
SD	0,00	31,02	2,40	0,38	0,38	1,53
CV %	0	14	17	4	6	5
Variation versus not heparinoid added PRP %	100	-83	-92	133	157	66
Variation versus Enoxaparine added PRP %	-9	-52	-55	-6	-4	1
DIA2844->=Hexadecasaccharides	4	113	8,15	10	6	28
DIA2844->=Hexadecasaccharides	4	126	9,35	11	7	29
DIA2844->=Hexadecasaccharides	4,5	108	7,79	11	6,5	31
Mean	4,17	115,67	8,43	10,67	6,50	29,33
SD	0,29	9,29	0,82	0,58	0,50	1,53
CV %	7	8	10	5	8	5
Variation versus not heparinoid added PRP %	138	-91	-96	151	160	50
Variation versus Enoxaparine added PRP %	9	-75	-74	2	-3	-3

Figure 2

ETP
[Heparinoïd] = 5 µg/mL

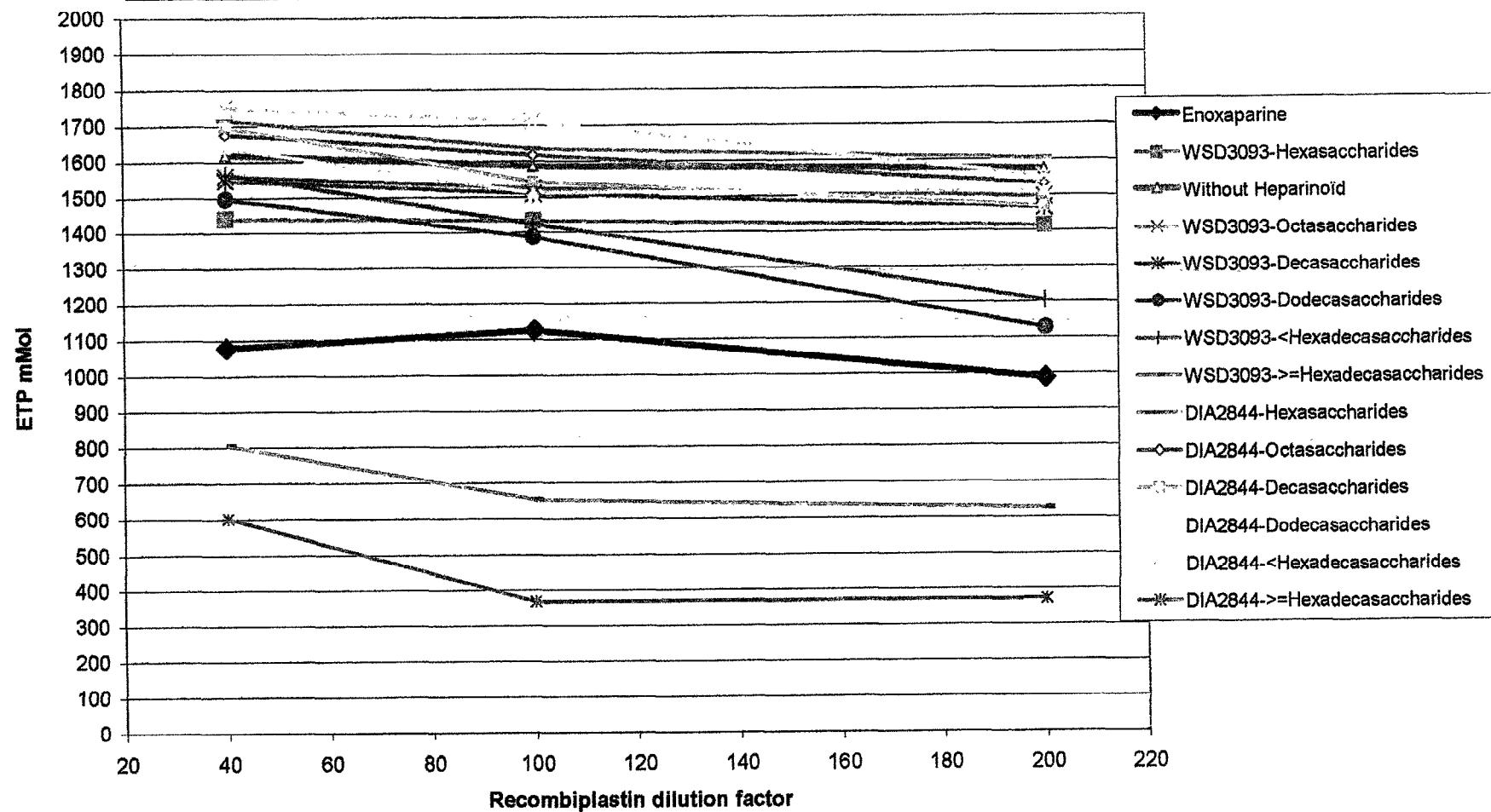


Figure 3

LAG TIME (Min)
Hemoliance Recombiplastin 1/100 diluted

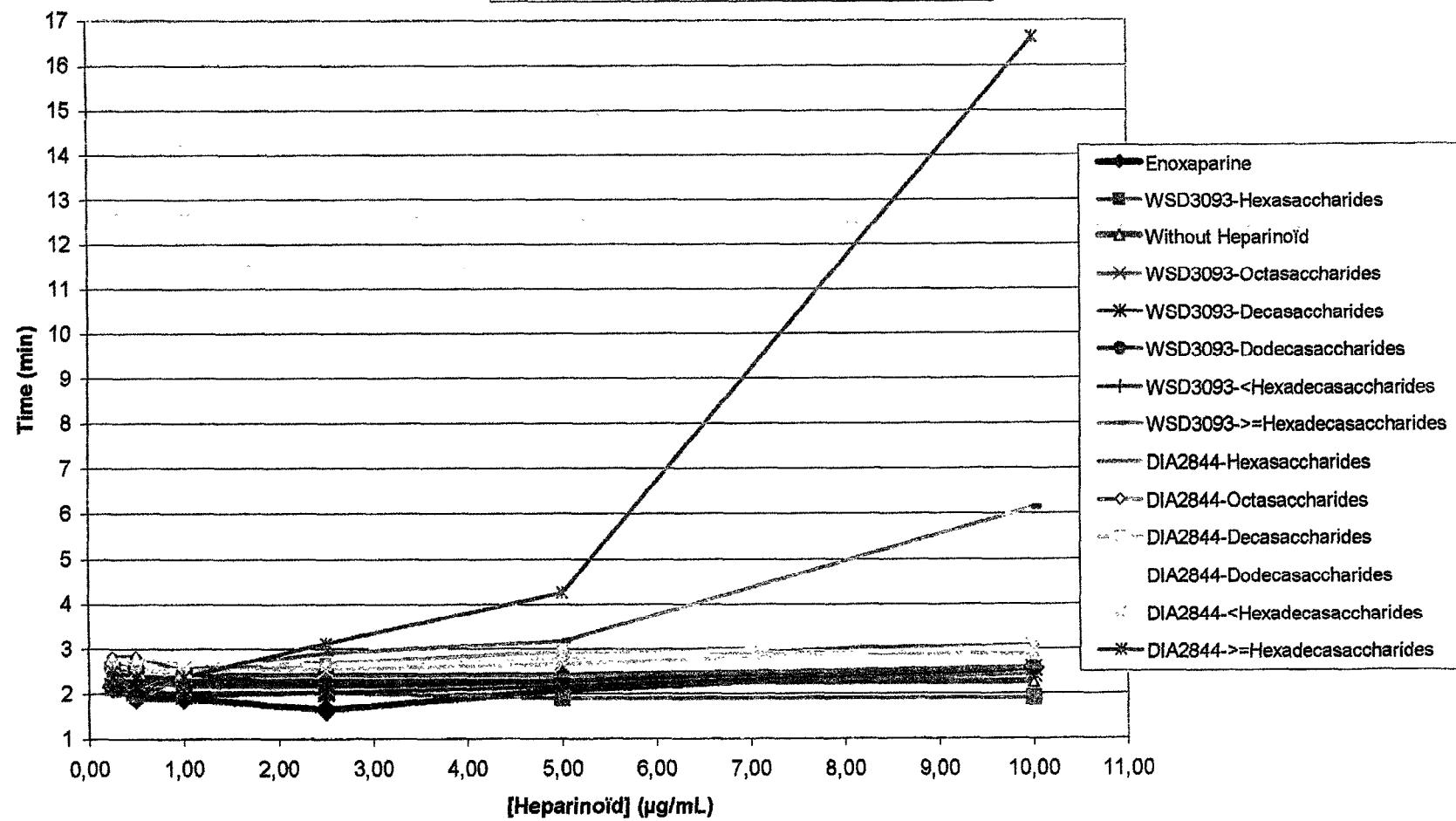


Figure 4

ETP
Hemoliance Recombiplastin 1/100 diluted

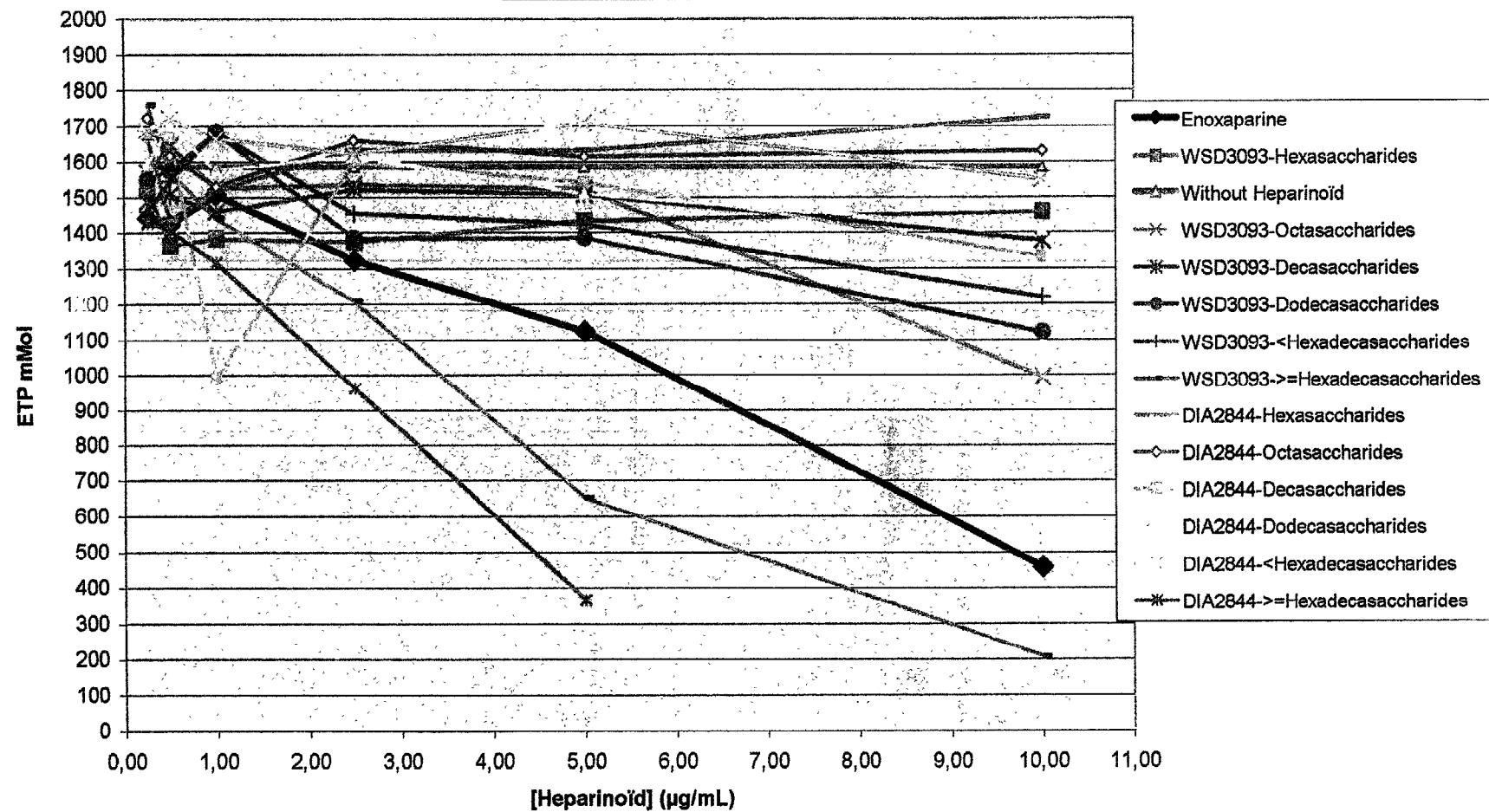


Figure 5

PEAK
Hemoliance Recombiplastin 1/100 diluted

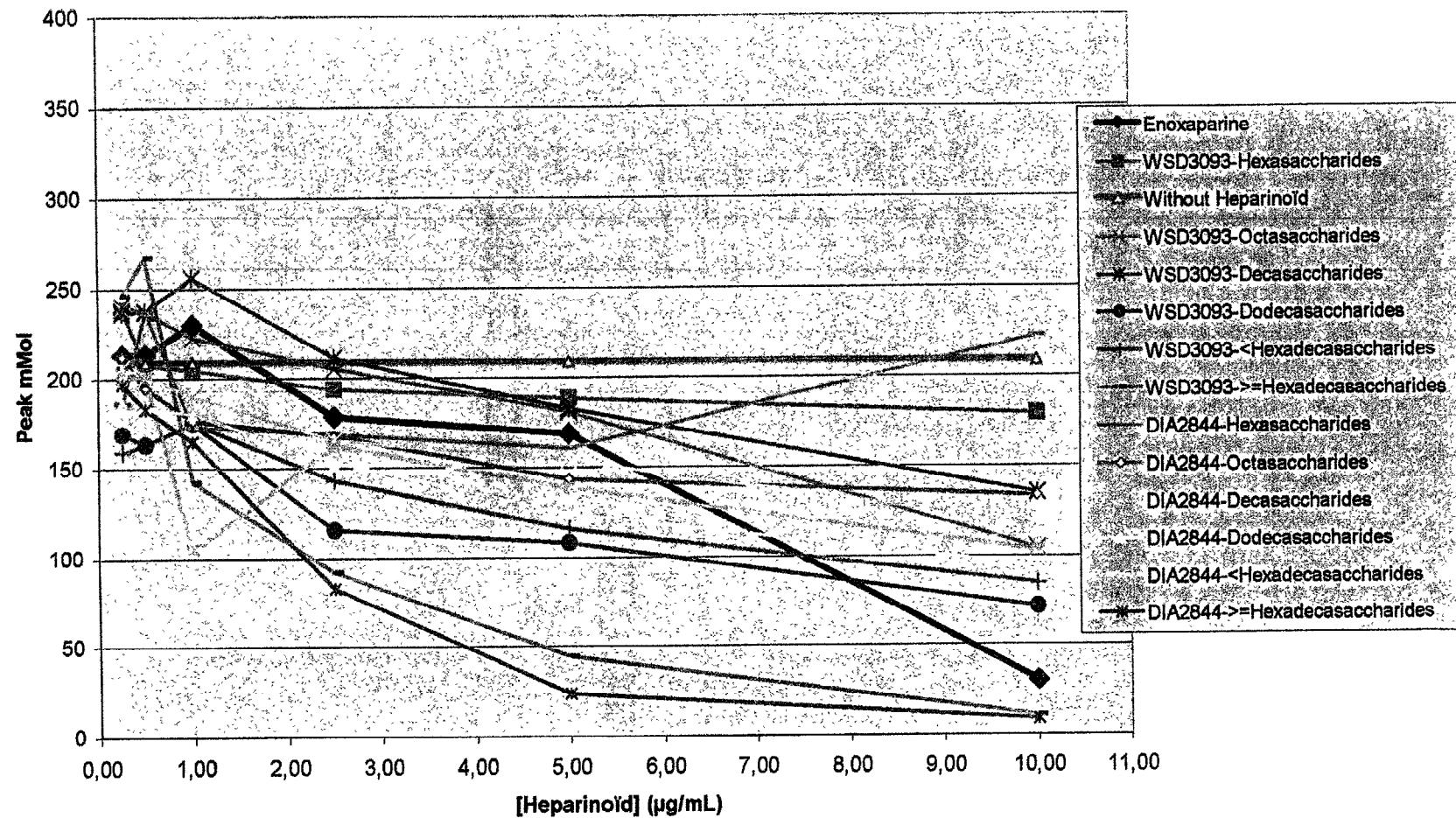


Figure 6

TIME TO PEAK
Hemoliance Recombiplastin 1/100 diluted

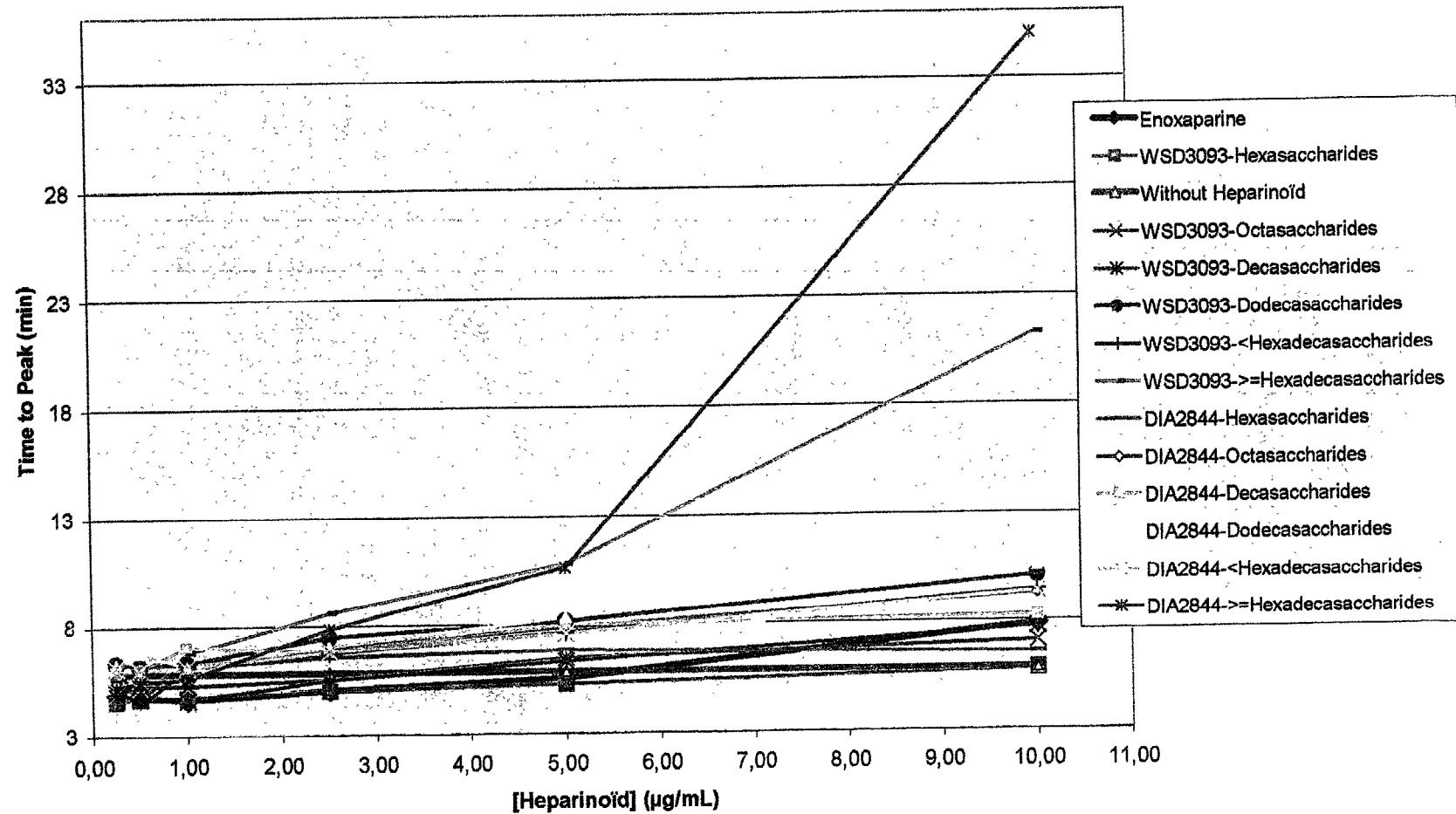
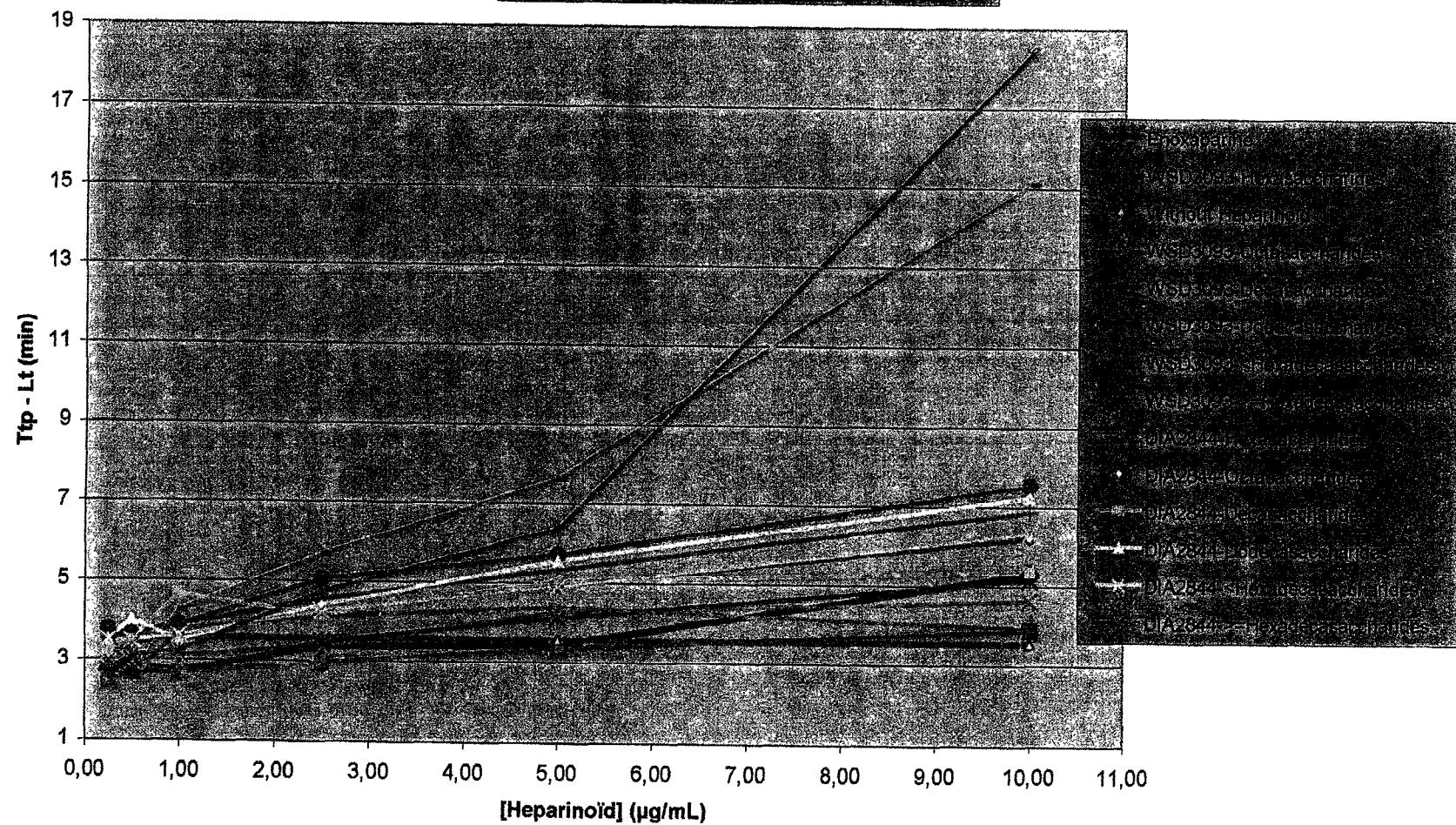


Figure 7

NUANCES PEAK - EACH TIME
Heparinoid group desirous of heparin



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Figure 8

START TAIL
Hemoliance Recombiplastin 1/100 diluted

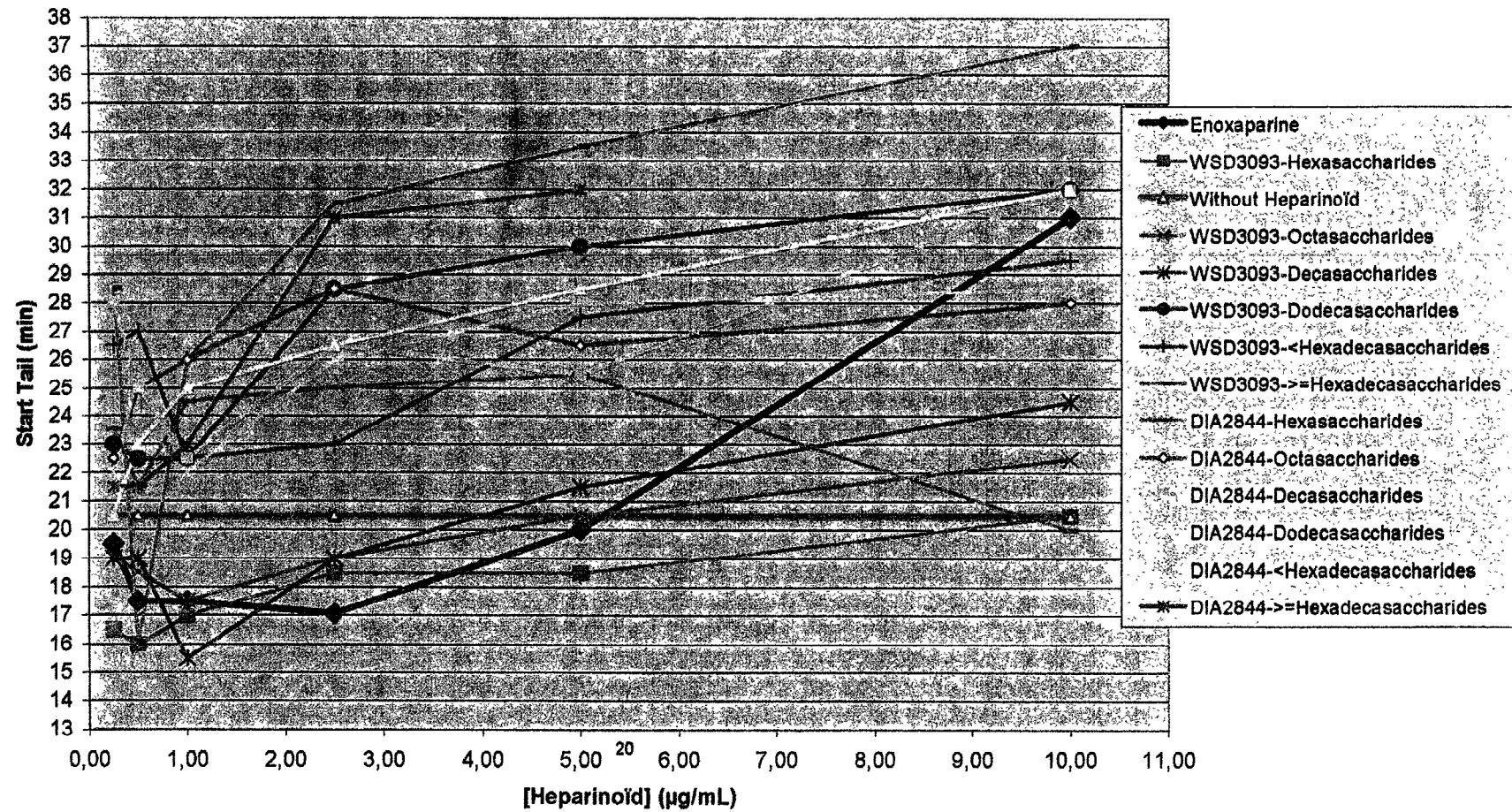


FIGURE 9

LAG TIME
Hemoliance Recombiplastin 1/100 diluted

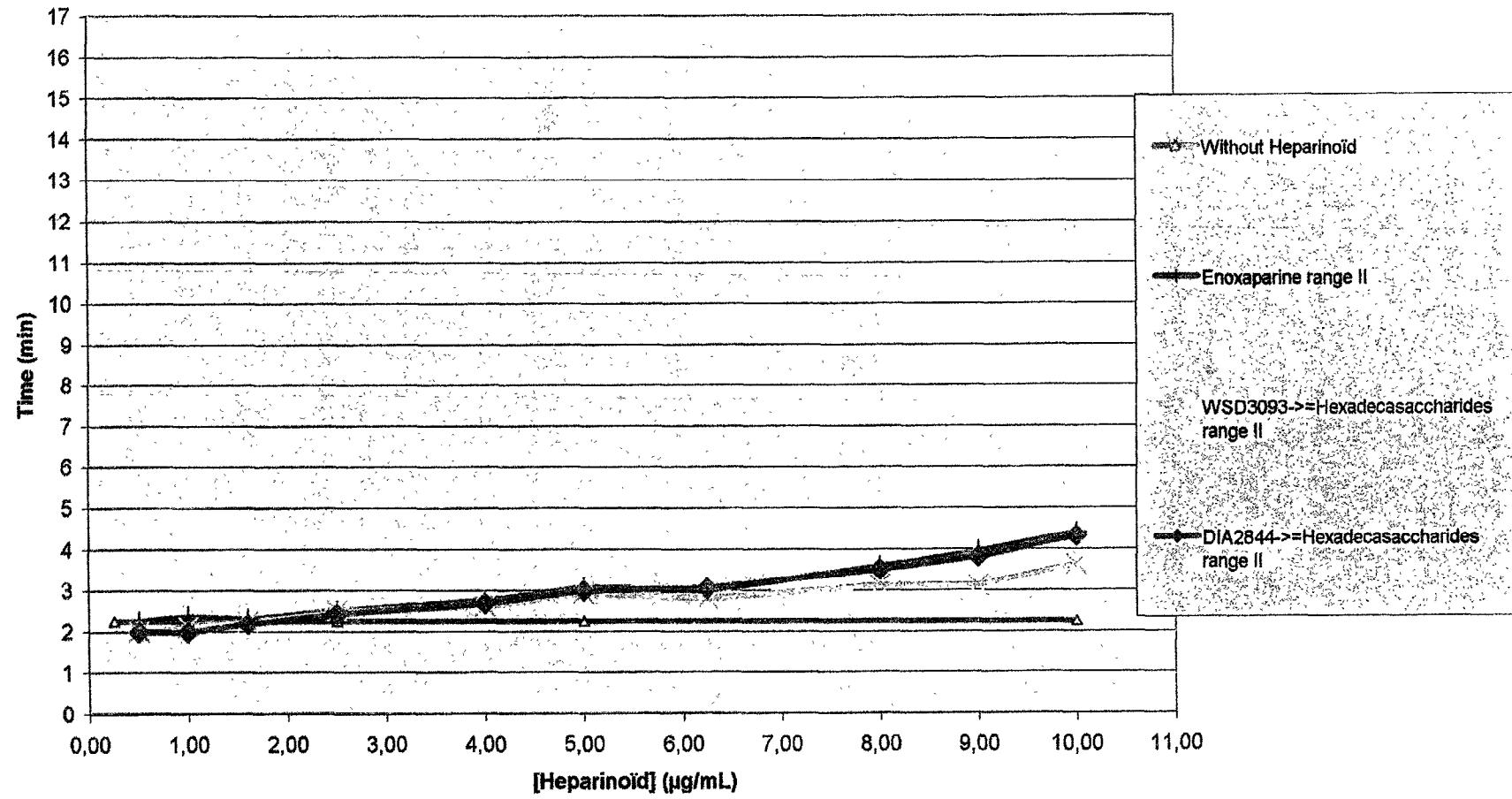


FIGURE 10

Subject II
LAG TIME
Hemoliance Recombiplastin 1/100 diluted

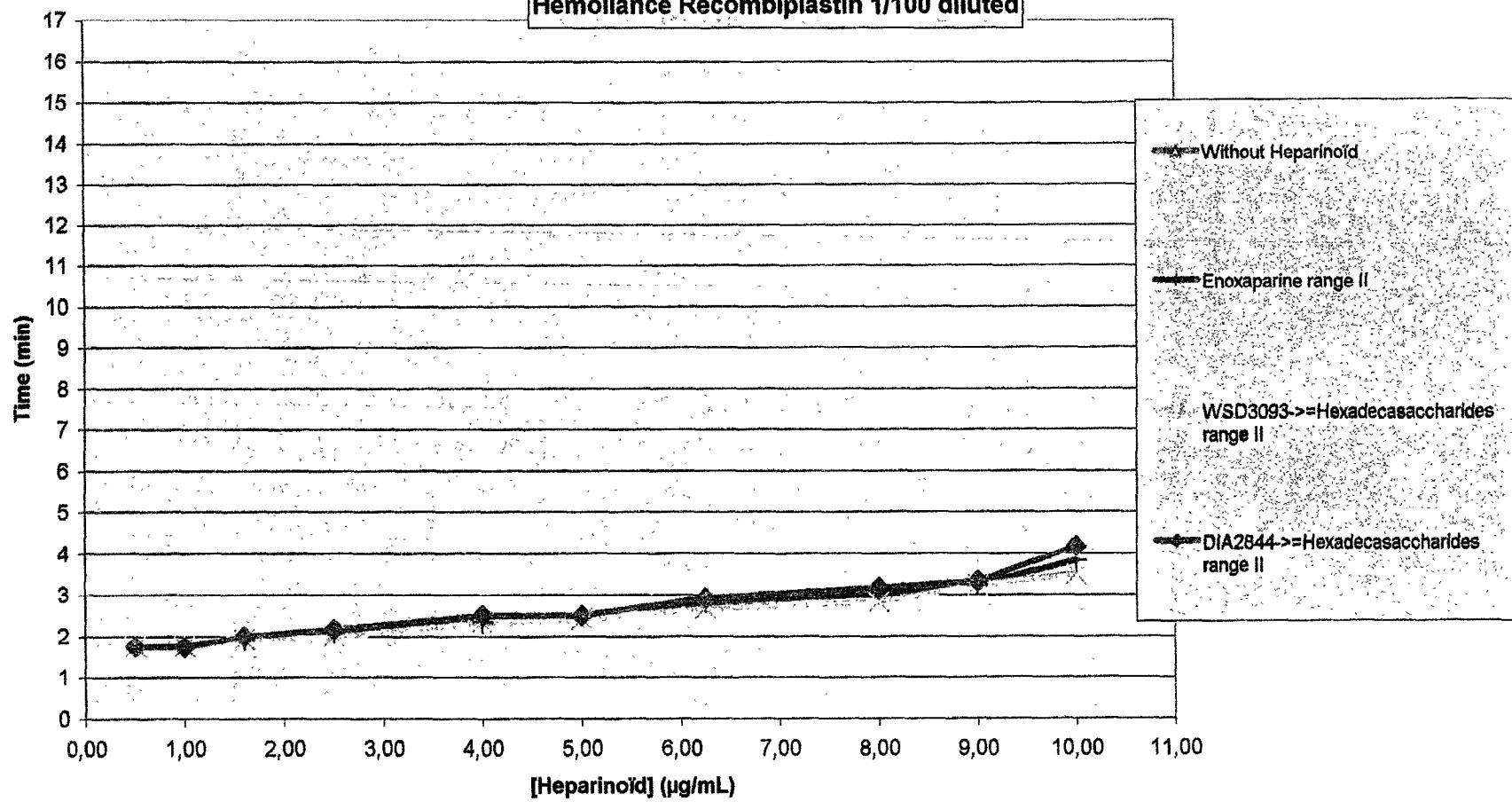


FIGURE 11

ETP
Hemoliance Recombiplastin 1/100 diluted

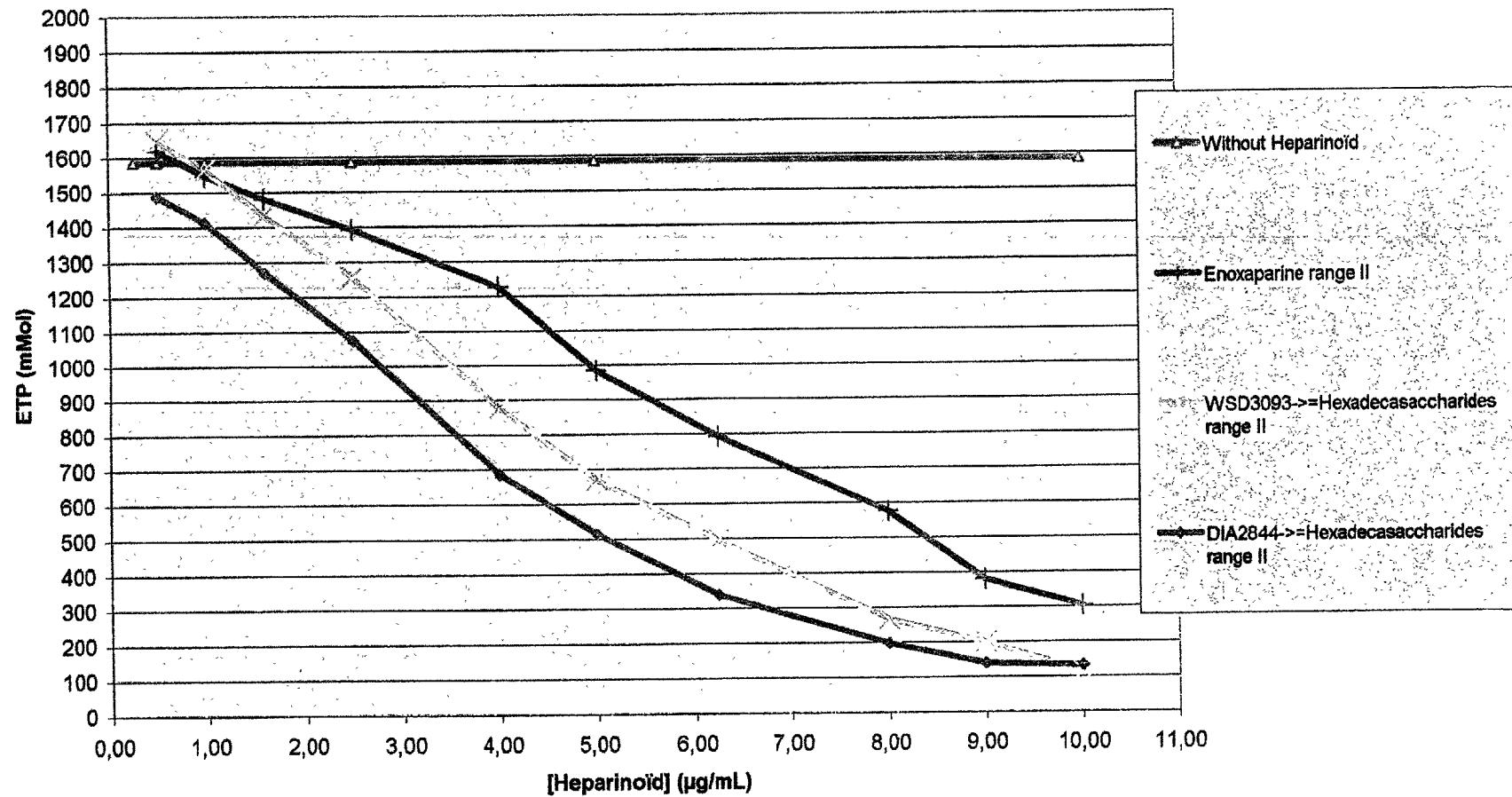


FIGURE 12

Subject II
ETP
Hemoliance Recombiplastin 1/100 diluted

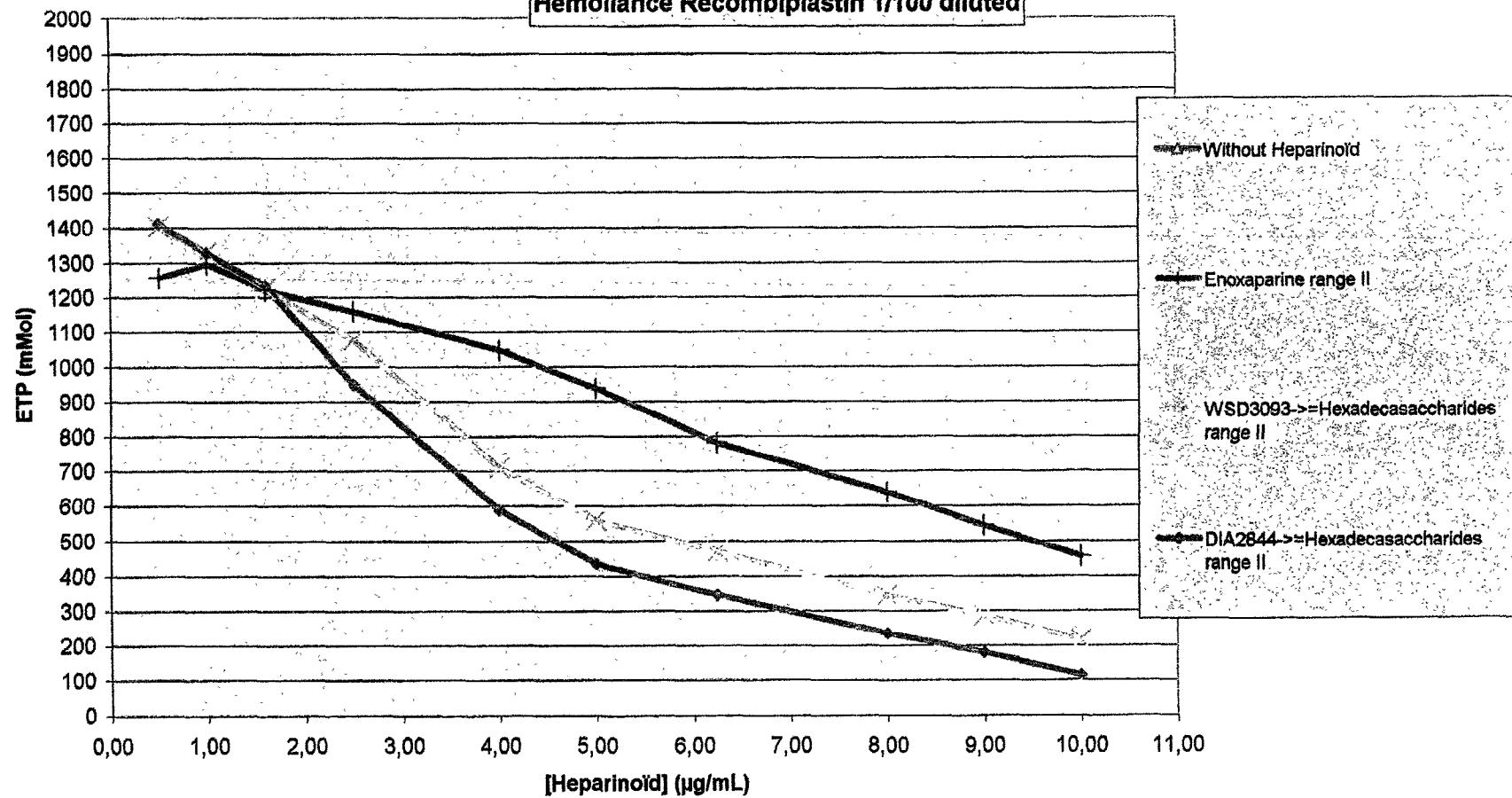


FIGURE 13

PEAK
Hemoliance Recombiplastin 1/100 diluted

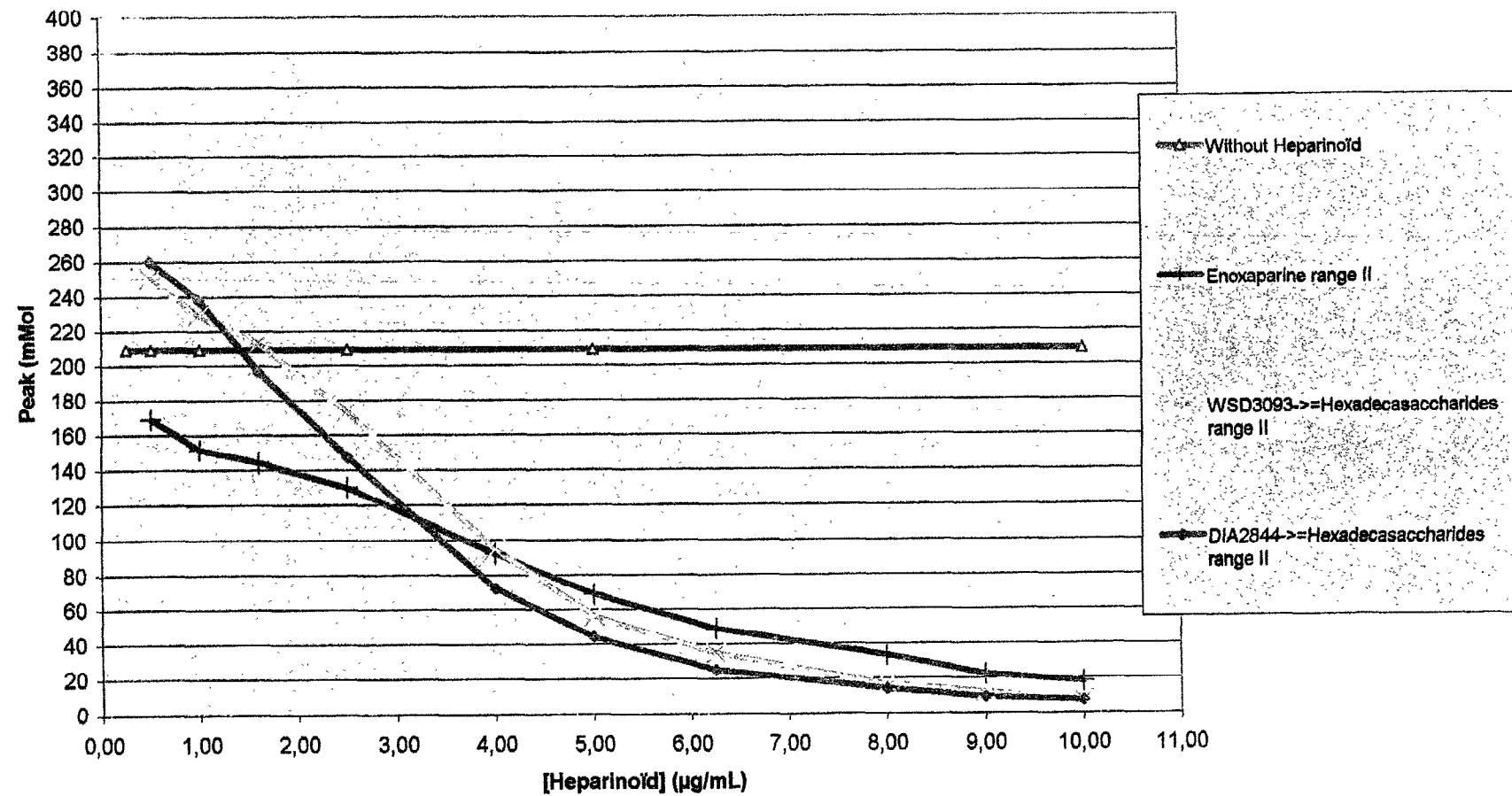


FIGURE 14

Subject II
PEAK
Hemoliance Recombiplastin 1/100 diluted

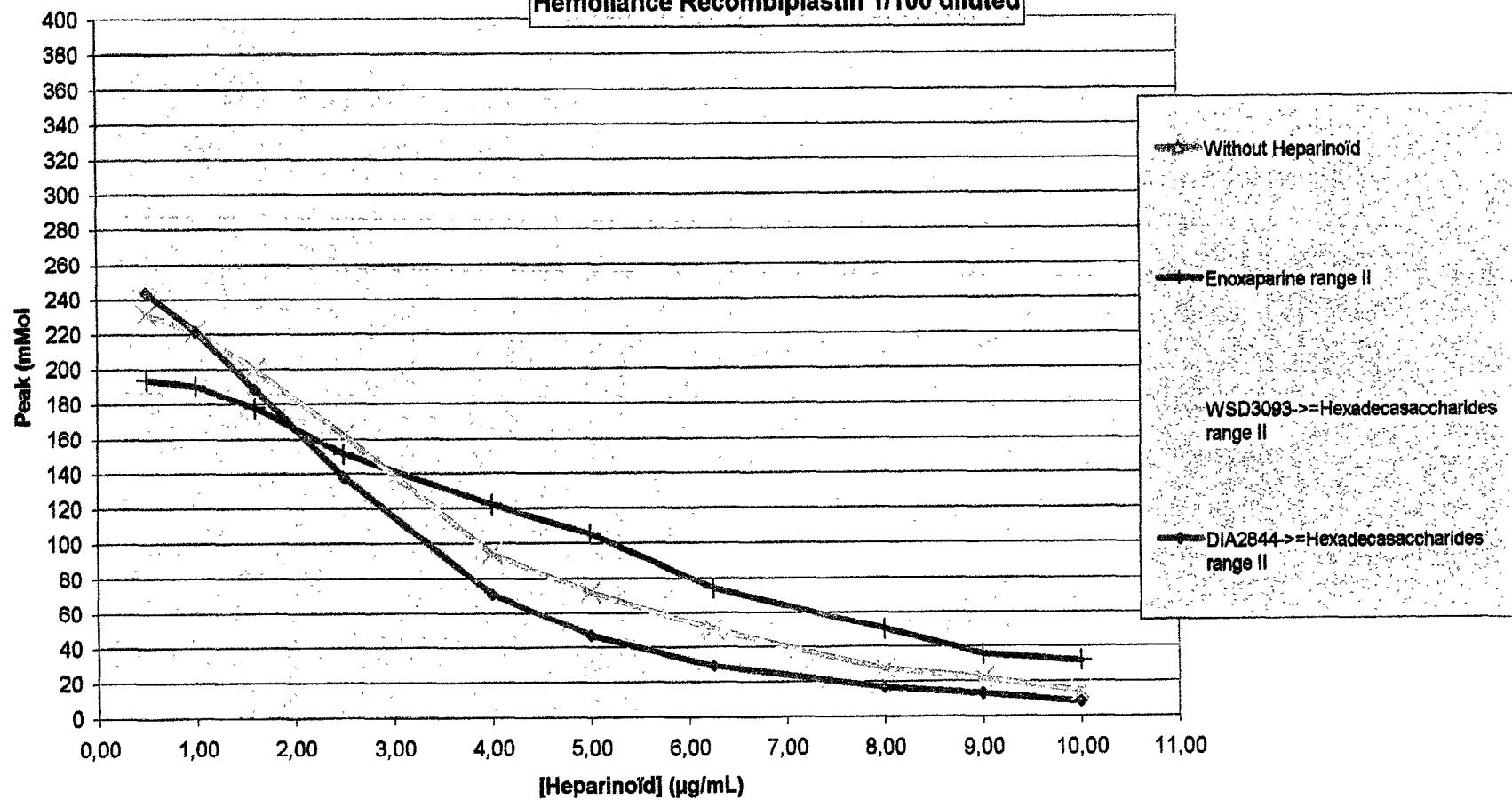
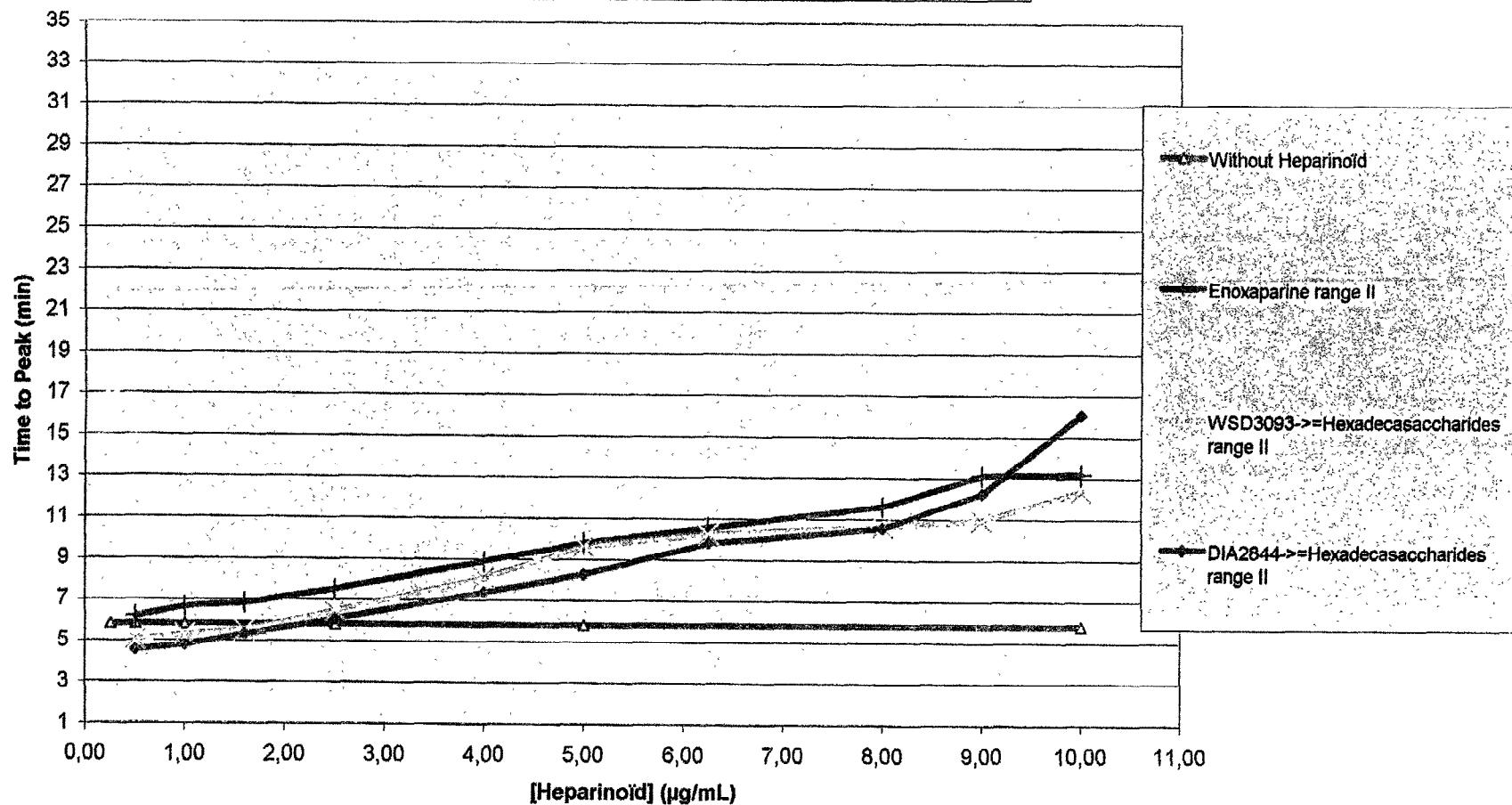


FIGURE 15

TIME TO PEAK
Hemoliance Recombiplastin 1/100 diluted



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FIGURE 16

Subject II
TIME TO PEAK
Hemoliance Recombiplastin 1/100 diluted

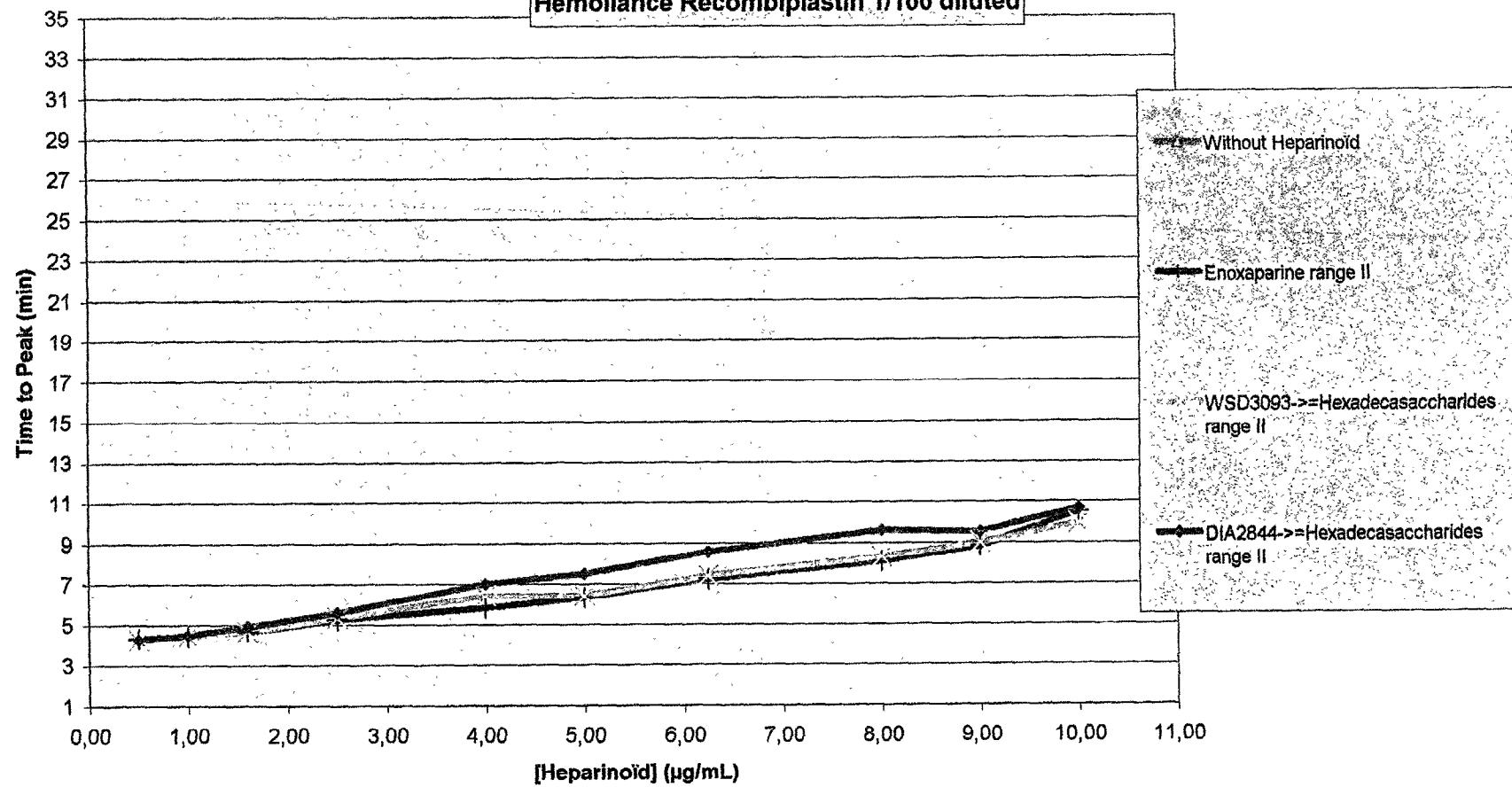


FIGURE 17

TIME TO PEAK - LAG TIME
Hemoliance Recombiplastin 1/100 diluted

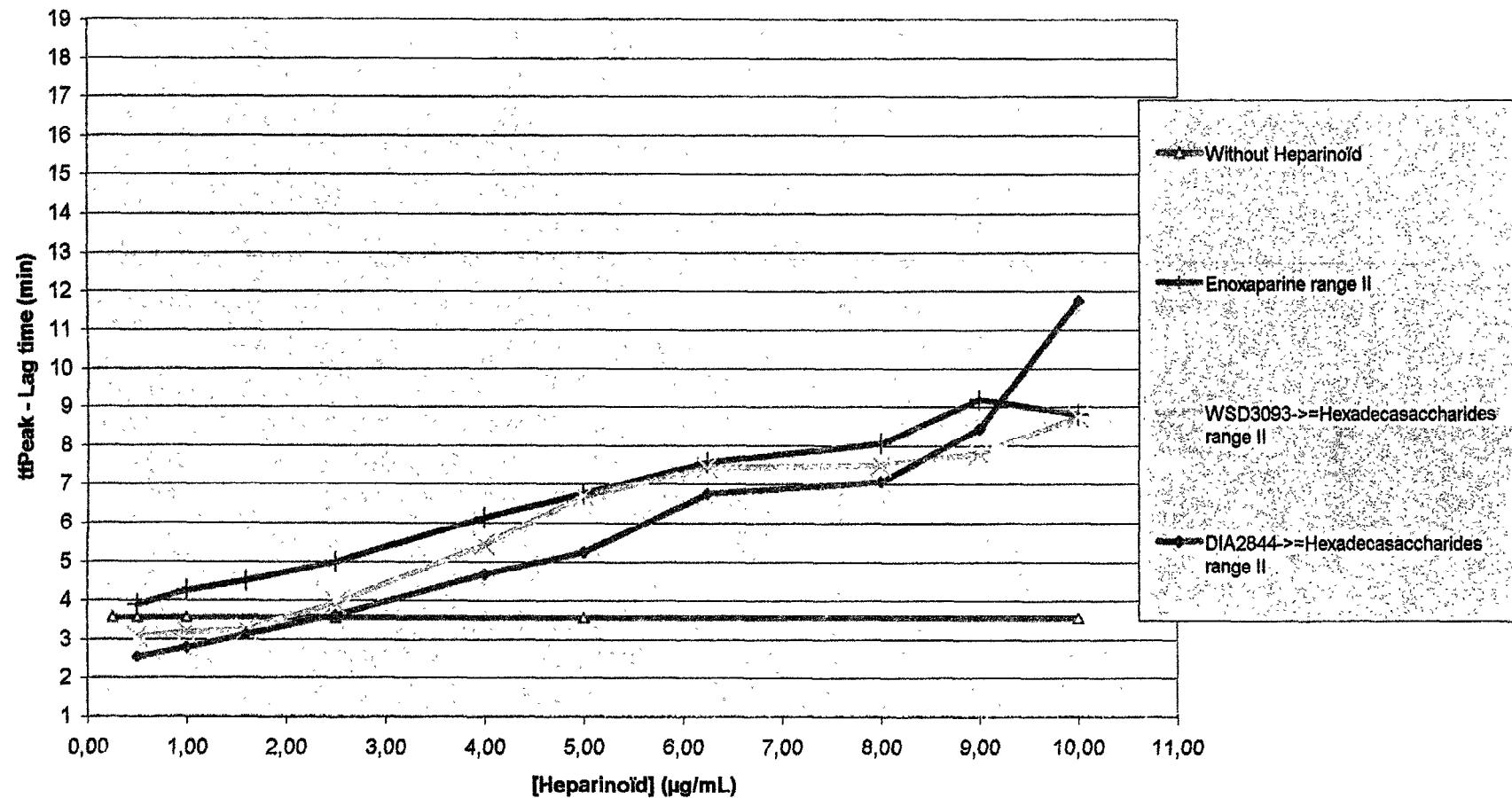


FIGURE 18

Subject II
TIME TO PEAK - LAG TIME
Hemoliance Recombiplastin 1/100 diluted

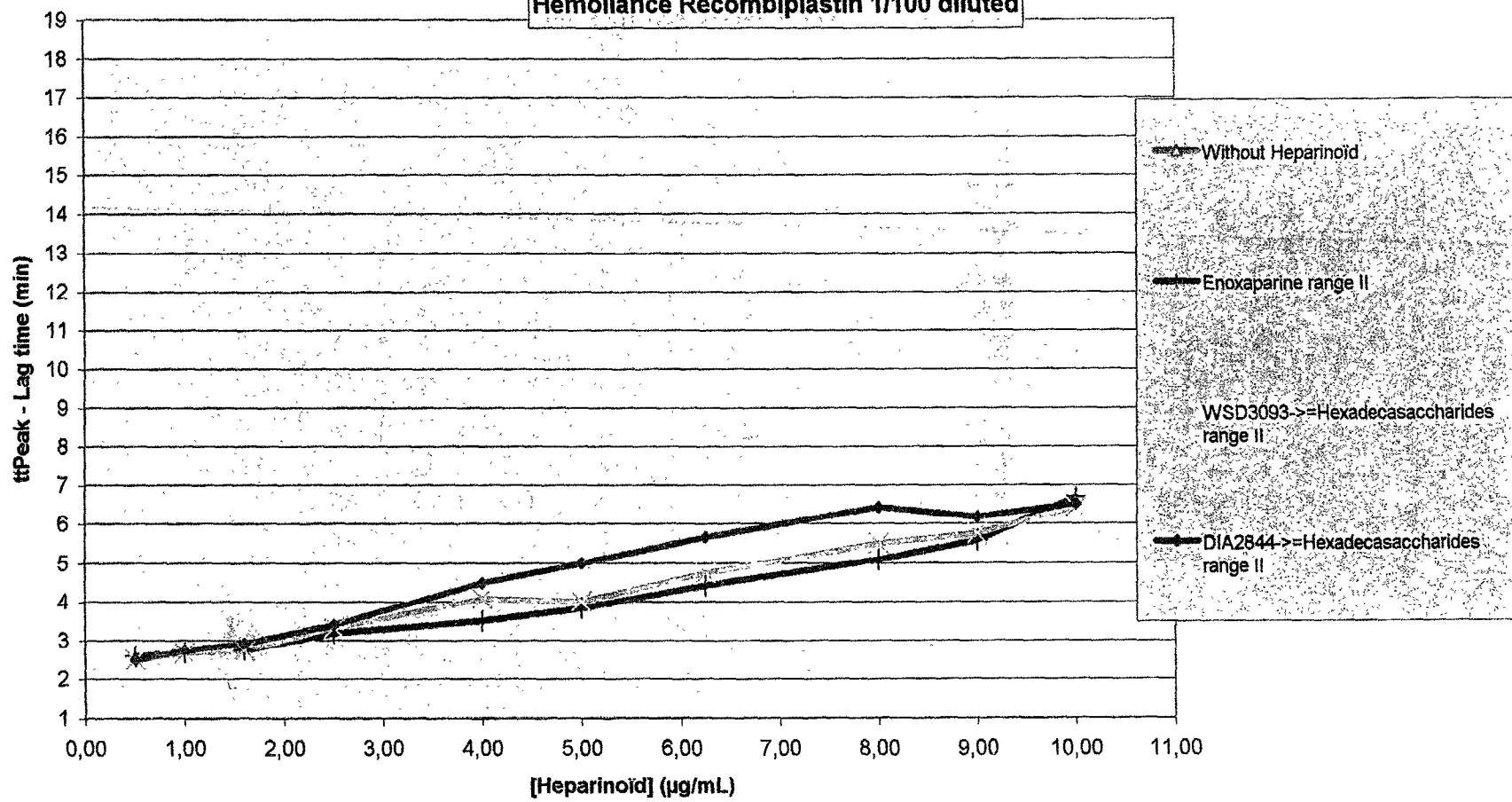


FIGURE 19

START TAIL
Hemoliance Recombiplastin 1/100 diluted

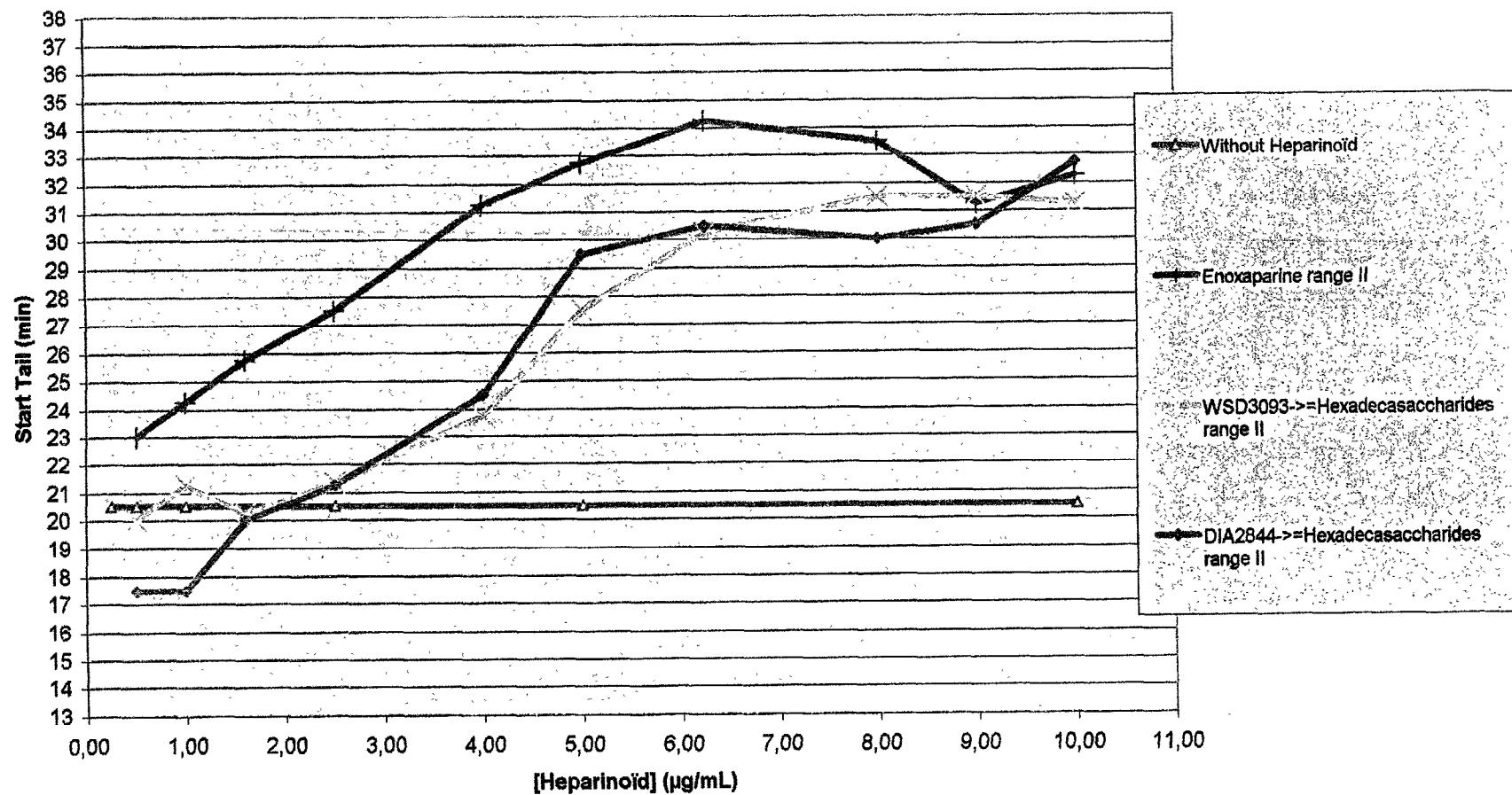


FIGURE 20

Subject II
START TAIL
Hemoliance Recombiplastin 1/100 diluted

